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ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

Sponsor: U.S. Army Medical Materiel
Development Activity

Contract No.: DAMD17-92-C-2001

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Test Articles: WR242511 Tartrate
WR269410

DRAFT

Study Director

Barry S. Levine, D.Sc., D.A.B.T.

In-Life Phase Completed On

July 14, 1993

Performing Laboratory

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<p>This study examined the acute oral and intraperitoneal toxicity of WR242511 tartrate and WR269410 in rats. The dose levels were selected on the basis of range-finding tests. After dosing, the animals were weighed weekly, observed daily for 14 days, and the survivors were necropsied on Day 14. Nonsurvivors were also necropsied. The acute oral LD50 of WR242511 tartrate in male rats, administered in 1% Methylcellulose/0.4% Tween 80 by gavage, was approximately eight-fold lower than in female rats (males; 16.3 mg base/kg and females; 135 mg base/kg). The LD50 values obtained when WR242511 tartrate was administered intraperitoneally in the same vehicle were not significantly different between the sexes (males; 32 mg base/kg and females; 30 mg base/kg). Thus, the LD50 of WR242511 tartrate was unaffected by sex when administered by intraperitoneal injection, but affected by sex when administered orally. The acute oral LD50 of WR269410 in male rats, administered in 1% Methylcellulose/0.4% Tween 80 by gavage, was approximately four-fold greater than in female rats (males; 603 mg/kg and females; 147 mg/kg). Due to a physical inability to intraperitoneally administer WR269410 dosage formulations in 0.1% Methylcellulose/0.4% Tween 80 at high enough concentrations to produce lethality, WR269410 was administered intraperitoneally as a solution in polyethylene glycol 200 (PEG 200). The calculated LD50 value of intraperitoneally administered WR269410 in males was 155 mg/kg. An LD50 value in females was estimated to be approximately 70 - 80 mg/kg. The results of this study suggest that WR242511 tartrate is more acutely toxic than WR269410 when administered either orally or intraperitoneally. Based on the oral LD50 data and after consultation with the Sponsor, the following dose levels are suggested to be used in the two week oral dose range-finding studies in rats of WR242511 tartrate; 0, 0.5, 2.0, and 6.2 mg base/kg/day, and of WR269410; 0, 2.0, 6.0, 18.0 mg/kg/day.</p>						
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STATEMENT OF COMPLIANCE

To the best of my knowledge, (Study No. 104 - ACUTE ORAL AND INTRAPERITONEAL TOXICITY STUDY OF WR242511 AND WR269410 IN RATS) was conducted in compliance with the Good Laboratory Practices regulations as published in 21 CFR 58, 40 CFR 160 and 40 CFR 792 in all material aspects with the following reservations:

The stability of the test or control articles under the test conditions has not been determined by the testing facility (Sections 105 and 185). This requirement is not applicable since only a single dose was administered in this study. Test article stability will be reported following completion of the repeat dose toxicity studies.

The protocol for this study was approved by the UIC Animal Care Committee.

Signature

Study Director

Barry S. Levine, D.Sc., D.A.B.T.

Date

QUALITY ASSURANCE STATEMENT

STUDY TITLE: ACUTE ORAL AND INTRAPERITONEAL TOXICITY STUDY OF
WR242511 AND WR264910 IN RATS

STUDY NUMBER: 104

STUDY DIRECTOR: BARRY S. LEVINE

INITIATION DATE: 12/3/92

This study has been divided into a series of phases. Using a random sampling approach, Quality Assurance monitors each of these phases over a series of studies. Procedures, equipment, documentation, etc., are examined in order to assure that the study is performed in accordance with the Good Laboratory Practice regulations of the Food and Drug Administration and the Environmental Protection Agency to assure that the study is conducted according to the protocol.

The following are the inspection dates, phases inspected, and report dates of QA inspections of the study.

INSPECT ON 12/7/92, TO STUDY DIR 12/7/92, TO MGMT 12/7/92
PHASES: PROTOCOL REVIEW

INSPECT ON 5/13/93, TO STUDY DIR 5/13/93, TO MGMT 5/13/93
PHASES: ROOM ENVIRONMENT, QUARANTINE AND LICK-IT CHECK

INSPECT ON 5/27/93, TO STUDY DIR 5/27/93, TO MGMT 5/28/93
PHASES: BODY WEIGHT, DOSING AND CLINICAL SIGNS

INSPECT ON 7/20/93, TO STUDY DIR 7/22/93, TO MGMT 7/23/93
PHASES: ANALYTICAL LABORATORY RAW DATA AND REPORT AUDIT

INSPECT ON 9/2-3/93, TO STUDY DIR 9/10/93, TO MGMT 9/14/93
PHASES: RAW DATA

INSPECT ON 9/8-10/93, TO STUDY DIR 9/10/93, TO MGMT 9/14/93
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9/13/93
DATE

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ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

TRL Chemical Nos.: 1620614 & 1720614

Sponsor: U.S. Army Medical Materiel
Development Activity
Frederick, MD 21702-5009

Test Articles: WR242511 Tartrate
WR269410

Sponsor
Representative: George J. Schieferstein, Ph.D.

Testing Facility: Toxicology Research Laboratory (TRL)
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Barry S. Levine, D.Sc., D.A.B.T. Date

Dosing Initiation: May 27, 1993

In-Life Completion: July 14, 1993

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1. SUMMARY

This study examined the acute oral and intraperitoneal toxicity of WR242511 tartrate and WR269410 in rats. The dose levels were selected on the basis of range-finding tests. After dosing, the animals were weighed weekly, observed daily for 14 days, and the survivors were necropsied on Day 14. Nonsurvivors were also necropsied.

As shown in Table 1, the acute oral LD50 of WR242511 tartrate in male rats, administered in 1% Methylcellulose/0.4% Tween 80 by gavage, was approximately eight-fold lower than in female rats (males; 16.3 mg base/kg and females; 135 mg base/kg). The LD50 values obtained when WR242511 tartrate was administered intraperitoneally in the same vehicle were not significantly different between the sexes (males; 23 mg base/kg and females; 30 mg base/kg). Thus, the LD50 of WR242511 tartrate was unaffected by sex when administered by intraperitoneal injection, but affected by sex when administered orally.

The acute oral LD50 of WR269410 in male rats, administered in 1% Methylcellulose/0.4% Tween 80 by gavage, was approximately three-fold greater than in female rats (males; 420 mg/kg and females; 147 mg/kg). Due to a physical inability to intraperitoneally administer WR269410 dosage formulations in 0.1% Methylcellulose/0.4% Tween 80 at high enough concentrations to produce lethality, WR269410 was administered intraperitoneally as a solution in polyethylene glycol 200 (PEG 200). The calculated LD50 value of intraperitoneally administered WR269410 in males was 155 mg/kg (Table 1). An LD50 value in females was estimated to be approximately 70 - 80 mg/kg.

The results of this study suggest that WR242511 tartrate is more acutely toxic than WR269410 when administered either orally or intraperitoneally. Based on the oral LD50 data and after consultation with the Sponsor, the following dose levels are suggested to be used in the two week oral dose range-finding studies in rats of WR242511 tartrate; 0, 0.5, 2.0, and 6.2 mg base/kg/day, and of WR269410; 0, 2.0, 6.0, 18.0 mg/kg/day.

2. INTRODUCTION

The purpose of this study was to assess the toxicity of the WR242511 tartrate and WR269410 in CD® rats following a single oral or intraperitoneal dose. The results of this study will be used to select dose levels for a two week oral dose range-finding study in rats for both test articles. The experimental design was based on the Sponsor's requirements. The protocol for this study was approved by the UIC Animal Care Committee. The rat is a standard and accepted species for toxicology studies, and was specified by the Sponsor. The routes were also specified by the Sponsor. No unforeseen circumstances affected the integrity of the study. Dosing was initiated on May 27, 1993 and the in-life portion was terminated on July 14, 1993.

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3. MATERIALS AND METHODS

3.1 Test Articles

One test article (WR242511 Tartrate, Bottle No. BM05816, Lot No. DJD-08-235), a yellow, crystalline powder, was received on December 15, 1992 from Herner & Co. and was assigned an in-house chemical number (1720614). It was stored in the original container at -20 to -15°C and at the ambient relative humidity of the freezer protected from light. The Analytical Chemistry Report is contained in Appendix 1. The test article was initially identified by GC-MS and the purity was determined by HPLC ($99.51 \pm 0.02\%$).

The second test article (WR269410, Bottle No. BM11565, Lot No. 866.B.91.1), an off-white powder, was received on December 15, 1992 from Herner & Co. and was assigned an in-house chemical number (1620614). It was stored in the original container at -20 to -15°C and at the ambient relative humidity of the freezer protected from light. The Analytical Chemistry Report is contained in Appendix 1. The test article was initially identified by GC-MS and the purity was determined by HPLC (100 %). For intraperitoneal studies, a formulation of the test article [WR269410 in Polyethylene Glycol 200 (PEG 200); concentration 100 mg/ml] was received on April 27, 1993 from Dr. Douglas R. Flanagan, University of Iowa, College of Pharmacy. It was stored in the original container at 0 - 4°C and at the ambient relative humidity of the refrigerator. WR269410 in PEG 200 was administered by the intraperitoneal route only. The concentration of two separate batches of the received test article in PEG 200 was determined to be 99.95 and 99.5 mg/ml by Dr. Flanagan, and is documented in Appendix 2.

3.2 Dosage Formulations

WR242511 tartrate was administered as a suspension using 1% Methylcellulose/0.4% Tween 80 as the vehicle. The dose levels and formulation concentrations of WR242511 tartrate in this report refer to quantities of base, not tartrate salt. WR269410 was orally administered as a suspension using 1% Methylcellulose/0.4% Tween 80 as the vehicle. Initially, in the range-finding test, WR269410 was administered intraperitoneally in 1% methylcellulose/0.4% Tween 80, but because suspensions of WR269410 necessary to produce mortality could not be passed through needles to dose the rats, following discussions with the Sponsor, the drug was administered as a solution in PEG 200 intraperitoneally. Stock solutions of WR269410 (concentration 100 mg/ml) were received from Dr. Douglas R. Flanagan as described above. Samples of all WR242511 tartrate and WR269410 dosage formulations in 1% Methylcellulose/0.4% Tween 80 were analyzed for test article concentration prior to their use. Samples of WR269410 dosage formulations in PEG 200 were sent to Dr. Flanagan for analysis, but the analysis report of test article concentration shown in Appendix 2 was received subsequent to test

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article use. Therefore, because report analysis was not released prior to dosing, a few dosage formulations of WR269410 were used in the acute toxicity study by intraperitoneal administration that were not within 10% of their intended concentrations. The results of these analyses are summarized in Table 2. For subsequent LD50 calculations, the actual dose levels administered based on the assayed concentration of WR269410 were used.

3.3 Test System

Virus Antibody Free male and female CD® rats, approximately 6 weeks of age (Date of Birth: March 31, 1993), were obtained from Charles River Breeding Laboratories, Kingston, New York on May 12, 1993. A second set of Virus Antibody Free male and female CD® rats, approximately 6 weeks of age (Date of Birth: May 6, 1993), were also obtained from Charles River Breeding Laboratories, Kingston, New York on June 16, 1993. Upon arrival, the animals were sexed and examined to determine their health, and were assigned a study-unique quarantine/pretest number. They were individually housed in polycarbonate cages, with Anderson Bed-o-cob® bedding (Heinold Co., Kankakee, IL), which conformed to the upper weight range recommended in the *Guide for the Care and Use of Laboratory Animals*, DHHS (NIH) No. 86.23. Animal room temperature and relative humidity were generally maintained at 65 - 78 °F and 30 - 70%, respectively. The room was on a 14 hour light/10 hour dark cycle. The animals were transferred to clean cages once weekly.

The rats were provided *ad libitum* access to drinking water via an automatic watering system in which the room distribution lines were flushed daily, and to Purina Certified Rodent Chow No. 5002 (Ralston Purina Company, St. Louis MO) except for a 16 - 20 hour fast prior to oral dosing and until \approx 2 hours after dosing. The water was untreated with additional chlorine or HCl. The animals were quarantined for approximately one week prior to test article administration, except for the range-finding test which was conducted during the quarantine period. They were examined by the Clinical Veterinarian near the end of the quarantine period, and were released for placement on test at that time.

3.4 Experimental Design

The study was conducted in phases. The particular phases of the study are designated in the summary and the individual data as follows: (1) the study number, "104" in the first three digits; (2) the route, either "PO" (oral) or "IP" (intraperitoneal) in the next two digits; and (3) the test article, either "24" or "4" (WR242511 tartrate) or "26" or "6" (WR269410) in the last two or one digit(s). When additional dose levels were added to the study due to excessive mortality or a steep dose-mortality curve, the test article was designated by a single digit ("4" or "6") and the additional sets of animals are designated in the final digit as either "A" if one additional set of animals were used or

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as "A" and "B" if two additional sets of animals were used. These designations of using one letter to designate the test article and one letter to designate additional animal groups was used for WR242511 tartrate administered by gavage, WR242511 tartrate administered intraperitoneally, and WR269410 administered by gavage.

In range-finding tests, the selected animals were identified by their pretest number. A cage card appeared on the front of each cage and contained the following information: study number, animal number, test article identification, treatment group number and dose level. Oral dosing (gavage) was accomplished by the use of a rigid oral feeding needle in overnight fasted animals. In intraperitoneal tests, dosing was accomplished by the use of a 16 gauge x 1 inch needle. Body weights were obtained on Day 0 for dosing calculations. The animals were observed for clinical signs and mortality for at least 5 days. Survivors were euthanized and discarded. No post-mortem observations were conducted on these animals.

In the acute toxicity tests, at the end of the quarantine/pretest period, 5 animals/sex/group were chosen for the study using a computer generated-randomization program. The selected animals were uniquely identified by an ear tag. A cage card appeared on the front of each cage and contained the following information: study number, animal number, test article identification, treatment group number and dose level.

The test animals were given either a single oral dose or a single intraperitoneal dose of the appropriate concentration of the test article. Following an overnight fast (\approx 16 - 20 hours), oral dosing was accomplished by the use of a rigid oral feeding needle. The intraperitoneal dosing was accomplished by the use of a 16 gauge x 1 inch needle.

All animals were observed at least three times on Day 0 following test article administration (designated in the data as either "1, 2, or 3", or as "#1, #2 or #3" following the clinical sign of toxicity seen) and daily thereafter. Body weights were obtained in Week -1, and on Days 0, 7 and 14. All test animals which died were grossly necropsied as soon as possible. At fourteen days post-treatment (Day 14), all surviving animals were sacrificed by carbon dioxide and a gross necropsy was performed. The necropsy procedure was a thorough and systematic examination and dissection of the animal viscera and carcass. A veterinary pathologist was available to verify gross lesions. All tissues and organs were discarded following termination of the gross necropsy procedure.

The incidence of all pharmacologic and/or toxicological effects were calculated for each dose levels by sex. For body weights and body weight gains, means and standard deviations were calculated for each dose level by sex and time point. For the toxicity tests, probit analysis of dose-mortality data was used to calculate the LD50 and its 95% confidence interval (Litchfield and Wilcoxon, 1949).

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3.4A WR242511 Tartrate

3.4A.1 Range-Finding Test

3.4A.1.1 Gavage

Dose levels listed below were tested in the range-finding test.

<u>Dose Level</u> <u>(mg base/kg)</u>	<u>Dosage</u> <u>Formulation</u> <u>(mg/ml)</u>	<u>Dosing</u> <u>Volume</u> <u>(ml/kg)</u>	<u>No. of</u> <u>Males</u>	<u>No. of</u> <u>Females</u>
5	1	5	2	2
10	2	5	2	2
15	3	5	2	2
25	5	5	2	2
30	6	5	2	2
35	7	5	2	2
50	10	5	2	2
60	12	5	2	2
250	50	5	0	2
375	75	5	2	2

3.4A.1.2 Intraperitoneal

Dose levels listed below were tested in the range-finding test.

<u>Dose Level</u> <u>(mg base/kg)</u>	<u>Dosage</u> <u>Formulation</u> <u>(mg/ml)</u>	<u>Dosing</u> <u>Volume</u> <u>(ml/kg)</u>	<u>No. of</u> <u>Males</u>	<u>No. of</u> <u>Females</u>
25	25	1	2	2
125	125	1	2	2
250	250	1	0	2
500	500	1	2	2

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3.4A.2 Acute Toxicity Test

3.4A.2.1 Gavage

Based on the range-finding test, the following doses were administered.

<u>Treatment Group</u>	<u>Dose Level (mg base/kg)</u>	<u>Dosage Formulation (mg/ml)</u>	<u>Dosing Volume (ml/kg)</u>	<u>No. of Males</u>	<u>No. of Females</u>
1	10	2	5	5	0
2	15	3	5	5	0
3	20	4	5	5	5
4	25	5	5	5	0
5	35	7	5	5	0
6	50	10	5	5	5
7	110	22	5	0	5
8	250	50	5	0	5
9	600	120	5	0	5

The following set of animals (designated as 104PO4A) was subsequently added due to a steep dose-mortality curve.

<u>Treatment Group</u>	<u>Dose Level (mg base/kg)</u>	<u>Dosage Formulation (mg/ml)</u>	<u>Dosing Volume (ml/kg)</u>	<u>No. of Males</u>	<u>No. of Females</u>
1	16.5	3.3	5	5	0
2	18.0	3.6	5	5	0

3.4A.2.2 Intraperitoneal

Based on the range-finding test, the following were administered.

<u>Treatment Group</u>	<u>Dose Level (mg base/kg)</u>	<u>Dosage Formulation (mg/ml)</u>	<u>Dosing Volume (ml/kg)</u>	<u>No. of Males</u>	<u>No. of Females</u>
1	20	4	5	5	5
2	50	10	5	5	5
3	110	22	5	5	5
4	250	50	5	5	5
5	600	120	5	5	5

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The following set of animals (designated as 104IP4A) was subsequently added due to a higher incidence of mortality of WR242511 than expected.

<u>Treatment Group</u>	<u>Dose Level (mg base/kg)</u>	<u>Dosage Formulation (mg/ml)</u>	<u>Dosing Volume (ml/kg)</u>	<u>No. of Males</u>	<u>No. of Females</u>
1	5	1.0	5	5	5
2	10	2.0	5	5	5
3	16.5	3.3	5	5	5
4	30	6.0	5	5	5

3.4B WR269410

3.4B.1 Range-Finding Test

3.4B.1.1 Gavage

The following dose levels were tested in the range-finding test.

<u>Dose Level (mg/kg)</u>	<u>Dosage Formulation (mg/ml)</u>	<u>Dosing Volume (ml/kg)</u>	<u>No. of Males</u>	<u>No. of Females</u>
800	80	10	2	2
1000	100	10	2	2
1200	120	10	2	2
1600	160	10	2	2

3.4B.1.2 Intraperitoneal

The following dose levels were tested in the range-finding test.

<u>Dose Level (mg/kg)</u>	<u>*Dosage Formulation (mg/ml)</u>	<u>Dosing Volume (ml/kg)</u>	<u>No. of Males</u>	<u>No. of Females</u>
200	40	5	2	2
400	80	5	2	2
800	80	10	2	2
1600	160	10	-	-

*WR269410 in 0.1% Methylcellulose/0.4% Tween 80

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Dose Level (mg/kg)	Dosage *Formulation (mg/ml)	Dosing Volume (ml/kg)	No. of Males	No. of Females
0	0	5	0	1
0	0	10	1	0
50	10	5	2	2
150	30	5	2	2
250	50	5	2	2
375	37.5	10	2	2
500	50	10	2	2
500	100	5	2	2
1000	100	10	2	2

*WR269410 in Polyethylene Glycol 200

3.4B.2 Acute Toxicity Test

3.4B.2.1 Gavage

Based on the range-finding test, the following doses were administered. WR269410 was administered in two equal dosing volumes of 10 ml/kg approximately two hours apart. Water was withheld from animals in between the time of dosings.

Treatment Group	Dose Level (mg/kg)	Dosage Formulation (mg/ml)	Dosing Volume (ml/kg)	No. of Males	No. of Females
1	550	27.5	20	5	5
2	700	35.0	20	5	5
3	900	45.0	20	5	5
4	1150	57.5	20	5	5
5	1500	75.0	20	5	5

The following second set of animals (designated as 104PO6A) was subsequently added due to a high incidence of mortality of WR269410 than expected.

Treatment Group	Dose Level (mg/kg)	Dosage Formulation (mg/ml)	Dosing Volume (ml/kg)	No. of Males	No. of Females
1	150	7.5	20	0	5
2	230	11.5	20	5	5
3	350	17.5	20	5	5

The following third set of animals (designated as 104PO6B) was subsequently added when a higher incidence of mortality of WR269410 than expected was observed again.

<u>Treatment Group</u>	<u>Dose Level (mg/kg)</u>	<u>Dosage Formulation (mg/ml)</u>	<u>Dosing Volume (ml/kg)</u>	<u>No. of Males</u>	<u>No. of Females</u>
1	40	2.0	20	5	5
2	80	4.0	20	5	5
3	150	7.5	20	5	0

3.4B.2.2 Intraperitoneal

Based on the range-finding test, the following doses were administered.

<u>Treatment Group</u>	<u>Dose Level (mg/kg)</u>	<u>Dosage Formulation (mg/ml)</u>	<u>Dosing Volume (ml/kg)</u>	<u>No. of Males</u>	<u>No. of Females</u>
1	30	6	5	5	5
2	60	12	5	5	5
3	125	25	5	5	5
4	250	50	5	5	5
5	500	100	5	5	5

4. RESULTS

4.1 Range-Finding Test

4.1A WR242511 Tartrate

4.1A.1 Gavage

4.1A.1.1 Clinical signs

5 mg base/kg: rough coat, hunched posture, decreased activity
 10 mg base/kg: rough coat, hunched posture, decreased activity
 15 mg base/kg: rough coat, hunched posture, decreased activity, found dead
 25 mg base/kg: rough coat, found dead
 30 mg base/kg: rough coat, hunched posture, decreased activity, found dead
 35 mg base/kg: rough coat, hunched posture
 50 mg base/kg: rough coat, hunched posture, decreased activity, found dead
 60 mg base/kg: rough coat, hunched posture, decreased activity, found dead
 250 mg base/kg: rough coat, found dead (♀ only dosed)
 375 mg base/kg: rough coat, hunched posture, diarrhea, decreased activity, tremors, found dead

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4.1A.1.2 Mortality

<u>Dose Level (mg base/kg)</u>	<u>Mortality^a</u>	
	<u>Males</u>	<u>Females</u>
5	0/2	0/2
10	0/2	0/2
15	2/2	0/2
25	1/2	1/2
30	1/2	0/2
35	0/2	0/2
50	2/2	0/2
60	2/2	1/2
250	-	2/2
375	2/2	1/2

^anumber of deaths/number of animals in group.

4.1A.2 Intraperitoneal

4.1A.2.1 Clinical Signs

25 mg base/kg: rough coat
125 mg base/kg: rough coat, hunched posture, decreased activity, found dead
250 mg base/kg: rough coat, hunched posture, decreased activity, ataxia, found dead (♀ only dosed)
500 mg base/kg: rough coat, hunched posture, decreased activity, found dead

4.1A.2.2 Mortality

<u>Dose Level (mg base/kg)</u>	<u>Mortality^a</u>	
	<u>Males</u>	<u>Females</u>
25	0/2	0/2
125	1/2	0/2
250	-	1/2
500	2/2	2/2

^anumber of deaths/number of animals in group.

4.1B WR269410

4.1B.1 Gavage

4.1B.1.1 Clinical Signs

800 mg/kg: rough coat, hunched posture
1000 mg/kg: rough coat, blue feet, decreased activity, lethargic, ataxia, comatose, found dead
1200 mg/kg: lethargic, comatose, found dead
1600 mg/kg: rough coat, hunched posture, decreased activity, lethargic, comatose, found dead

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4.1B.1.2 Mortality

<u>Dose Level (mg/kg)</u>	<u>Mortality^a</u>	
	<u>Males</u>	<u>Females</u>
800	0/2	0/2
1000	1/2	2/2
1200	2/2	2/2
1600	1/2	2/2

^anumber of deaths/number of animals in group.

4.1B.2 Intraperitoneal

4.1B.2.1 Clinical Signs

WR269410 in 1% Methylcellulose/0.4% Tween 80

200 mg/kg: rough coat
400 mg/kg: rough coat
800 mg/kg: rough coat, hunched posture, decreased activity
1600 mg/kg: unable to dose animals

WR269410 in PEG 200

0 mg/kg: (5 ml/kg) rough coat, hunched posture, decreased activity (♀ only dosed)
0 mg/kg: (10 ml/kg) rough coat, hunched posture, decreased activity, lethargic (♂ only dosed)
50 mg/kg: rough coat, hunched posture, blue feet, labored breathing, decreased activity, lethargic
150 mg/kg: rough coat, hunched posture, blue feet, decreased activity, labored breathing, comatose, found dead
250 mg/kg: rough coat, hunched posture, labored breathing, decreased activity, lethargic, dark material on leg and food
375 mg/kg: rough coat, hunched posture, labored breathing, decreased activity, comatose, found dead
500 mg/kg: (5 ml/kg) rough coat, blue feet, lethargic, shallow breathing, labored breathing, comatose, found dead
500 mg/kg: (10 ml/kg) rough coat, hunched posture, blue feet, decreased activity, shallow breathing, lethargic, comatose, found dead
1000 mg/kg: found dead

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4.1B.2.2 Mortality

<u>Dose Level (mg/kg)</u>	<u>Mortality^a</u>	
	<u>Males</u>	<u>Females</u>
^b 200	0/2	0/2
400	0/2	0/2
800	0/2	0/2
^c 0 (5ml/kg)	-	0/1
0 (10ml/kg)	0/1	-
50	0/2	0/2
150	2/2	1/2
250	0/2	0/2
375	1/2	2/2
500 (5ml/kg)	2/2	2/2
500 (10ml/kg)	2/2	1/2
1000	2/2	2/2

^anumber of deaths/number of animals in group.

^bWR269410 in 1% Methylcellulose/0.4% Tween 80

^cWR269410 in PEG 200

4.2 Acute Toxicity Test

4.2A WR242511 Tartrate

4.2A.1 Gavage

4.2A.1.1 Dosage Formulation Analysis

Dosage formulation analysis is shown in Table 2 and is described with the analytical chemistry methodology in Appendix 1. All test article dosage formulations were within 10% of their intended concentration.

4.2A.1.2 Clinical Signs

A summary of clinical signs is shown in Tables 3 and 4 and individual data is shown in Appendix 3. Clinical signs of toxicity (hunched posture, decreased activity) were seen with increasing incidence as a function of dose levels in surviving animals. Rough coat was observed in all dose levels.

4.2A.1.3 Body Weight

A summary of body weights and body weight gains is shown in Tables 5 and 6; males and in Tables 7 and 8; females, and individual data for both sexes is shown in Appendix 4. In males, body weights and body weight gains were generally unaffected by test article treatment for those animals which survived the fourteen day observation period. At higher dose levels (110 mg base/kg and above), surviving females lost weight in the first week and their total weight gain was less than lower dose animals.

4.2A.1.4 Necropsy

The individual necropsy observations are in Appendix 5. Gross lesions observed in the WR242511 tartrate-treated males included: at 10 mg base/kg (red fluid in cranial cavity, splenic enlargement and liver enlargement); at 15 mg base/kg (liver enlargement, red fluid in cranial cavity, and splenic enlargement); at 16.5 mg base/kg (mottled lesions on kidney); at 20 mg base/kg (liver enlargement, red fluid in cranial cavity, and heart enlargement); at 25 mg base/kg (liver enlargement and mottled pigmentation); at 35 mg base/kg (liver enlargement, kidney enlargement, red fluid in cranial cavity, and mottled pigmentation); and at 50 mg base/kg (liver enlargement and mottled pigmentation, red fluid in cranial cavity, and kidney enlargement).

Gross lesions observed in females included: 20 mg base/kg (red fluid in the cranial cavity); at 110 mg base/kg (splenic enlargement); at 250 mg base/kg (red fluid in cranial cavity; splenic enlargement, liver enlargement, and kidney discoloration); and at 600 mg base/kg (red fluid in the cranial cavity).

4.2A.1.5 Mortality

Dose-mortality data are shown in Table 9. The oral LD50 (and its 95% confidence interval) of WR242511 tartrate for males are 16.3 (13.8 to 19.4) mg base/kg. The dose-mortality curve slope (probit/log dose) is 8.27. For females, the corresponding data are 135 (77 to 236) mg base/kg. The dose-mortality curve slope (probit/log dose) is 3.58. The LD50 and corresponding values were calculated by the method of Litchfield and Wilcoxon (1949) and is shown in Appendix 6.

4.2A.2 Intraperitoneal

4.2A.2.1 Dosage Formulation Analysis

Dosage formulation analysis is shown in Table 2 and is described with the analytical chemistry methodology in Appendix 1. All test article dosage formulations were within 10% of their intended concentration.

4.2A.2.2 Clinical Signs

A summary of clinical signs is shown in Tables 3 and 4 and individual data is shown in Appendix 3. Significant clinical signs of toxicity at lower doses included rough coat and hunched posture. Decreased activity, blue feet, and abdominal bloating were observed in increasing incidence in surviving animals as a function of dose level. Additionally, labored breathing, lethargy, and dark material on the face were also sporadically observed.

4.2A.2.3 Body Weight

A summary of body weights and body weight gains is shown in Tables 5 and 6; males and in Tables 7 and 8; females, and individual data for both sexes is shown in Appendix 4. In males, body weight loss was observed in all surviving animals except the two lowest dose levels in the first week, and body weight and total weight gains were less in these animals compared to the lower dose levels. In females, body weight and body weight gains were generally

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unaffected by test article treatment for those animals which survived the fourteen day observation period.

4.2A.2.4 Necropsy

The individual necropsy observations are in Appendix 5. Gross lesions observed in the WR242511 tartrate-treated males included: at 10 mg base/kg (scar on a liver); at 16.5 mg base/kg (scar on a liver); at 20 mg base/kg (red fluid in cranial cavity, dilation of cecum and colon, fluid in abdominal cavity, and enlargement of the adrenal glands); at 50 mg base/kg (red fluid in the cranial cavity and fluid in the abdominal cavity); at 110 mg base/kg (red fluid in the cranial cavity and fluid in the abdominal cavity); at 250 mg base/kg (red fluid in the cranial cavity, fluid in the abdominal cavity, and irregular pigmentation of a liver); and at 600 mg base/kg (red fluid in the cranial cavity, fluid in the abdominal cavity, and irregular pigmentation of the liver).

Gross lesions observed in the WR242511 tartrate-treated females include: at 5 mg base/kg (lesions on kidneys); at 10 mg base/kg (fluid in pericardium); at 16.5 mg base/kg (scar on a liver, adhesion on a liver and stomach dilation); at 20 mg base/kg (red fluid in cranial cavity, dilation of cecum and colon, fluid in abdominal cavity, irregular pigmentation of a liver and enlargement of the heart); at 30 mg base/kg (adhesions on the liver); at 50 mg base/kg (red fluid in the cranial cavity, fluid in the abdominal cavity and irregular liver pigmentation); at 110 mg base/kg (red fluid in the cranial cavity, fluid in the abdominal cavity and irregular pigmentation of liver); at 250 mg base/kg (red fluid in the cranial cavity, fluid in the abdominal cavity, splenic enlargement, hole in abdominal wall, and irregular pigmentation of a liver); and at 600 mg base/kg (red fluid in the cranial cavity, fluid in the abdominal cavity, and irregular pigmentation of a liver).

4.2A.2.5 Mortality

Dose-mortality data are shown in Table 9. The intraperitoneal LD50 of WR242511 tartrate for males is 23 mg base/kg with a 95% confidence interval of 14 to 37 mg base/kg. The dose-mortality curve slope (probit/log dose) is 2.68. The intraperitoneal LD50 of WR242511 tartrate for females is 30 mg base/kg with a 95% confidence interval of 14 to 66 mg base/kg. The dose-mortality curve slope (probit/log dose) is 1.49. The LD50 and corresponding values were calculated by the method of Litchfield and Wilcoxon (1949) and is shown in Appendix 6.

4.2B WR269410

4.2B.1 Gavage

4.2B.1.1 Dosage Formulation Analysis

Dosage formulation analysis is shown in Table 2 and Appendix 2. All test article dosage formulations were within 10% of their intended concentration.

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4.2B.1.2 Clinical Signs

A summary of clinical signs is shown in Tables 3 and 4 and individual data is shown in Appendix 3. Signs of toxicity observed in high dose animals included labored breathing, ataxia, comatose state, blue feet, and rough coat. In lower dose animals, rough coats, blue feet, hunched posture, and decreased activity (except of the lowest dose level) was seen in both sexes.

4.2B.1.3 Body Weight

A summary of body weights and body weight gains is shown in Tables 5 and 6; males and in Tables 7 and 8; females, and individual data for both sexes is shown in Appendix 4. All surviving animals gained weight, and Appendix 4), but surviving animals administered higher doses of WR269410 gained less weight than animals treated at lower dose levels.

4.2B.1.4 Necropsy

Individual necropsy data are in Appendix 5. Gross lesions observed in several of the WR269410-treated males include: at 550 mg/kg (lesions on a kidney and a spleen); at 700 mg/kg (lesions on a kidney); at 900 mg/kg (red fluid in cranial cavity and mottled pigmentation and enlargement of a liver); at 1150 mg/kg (lesions on a kidney); and at 1500 mg/kg (mottled pigmentation of a liver).

Gross lesions observed in several of the WR269410-treated females included: at 550 mg/kg (spots on lungs); and at 1500 mg/kg (red fluid in cranial cavity, mottled pigmentation of a liver, spots on a lung, and enlargement of the adrenal glands).

4.2B.1.5 Mortality

Dose-mortality data are shown in Table 9. The oral LD50 (and its 95% confidence interval) of WR269410 for males are 420 (219 to 806) mg/kg. The dose-mortality curve slope (probit/log dose) is 1.54. For females, the corresponding data are 147 (70 to 310) mg/kg. The dose-mortality curve slope (probit/log dose) is 1.44. The LD50 and corresponding values were calculated by the method of Litchfield and Wilcoxon (1949) and are shown in Appendix 6.

4.2B.2 Intraperitoneal

4.2B.2.1 Dosage Formulation Analysis

Dosage formulation analysis is shown in Table 2 and Appendix 2. Three of the five test article dosage formulations were outside of 10% of their intended concentration. The dosage formulation of 6.0 mg/ml, the 30 mg/kg treated animals, was administered in 15.0 % excess of its intended concentration. The dosage formulation of 12 mg/ml, the 60 mg/kg treated animals, was administered in 29.2 % deficiency of its intended concentration. Finally, the dosage formulation of 50.0 mg/ml, the 250 mg/kg treated animals, was administered in 14.2 % excess of its intended concentration. These dosage formulations were administered outside of their intended concentration because the results of the analysis were not released prior to dosing, as it was performed

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at the University of Iowa. Because these deviations would significantly affect the determination of LD50 values, the dose-mortality data utilized the actual dose levels administered rather than the intended dose levels, and the LD50s are determined from these values.

4.2B.2.2 Clinical Signs

A summary of clinical signs is shown in Tables 3 and 4 and individual data is shown in Appendix 3. Signs of toxicity (rough coat, hunched posture, blue feet, decreased activity, and lethargy) were observed in all treatment groups. Labored breathing and comatose state were primarily limited to the higher dose levels.

4.2B.2.3 Body Weight

A summary of body weights and body weight gains is shown in Tables 5 and 6; males and in Tables 7 and 8; females, and individual data for both sexes is shown in Appendix 4. Body weights and body weight gains were generally unaffected by test article treatment for those animals which survived the fourteen day observation period.

4.2B.2.4 Necropsy

The individual necropsy data are shown in Appendix 5. Gross lesions observed in the majority of WR269410-treated males included: at 30 mg/kg (irregular pigmentation or lesions on kidney, scarring on spleen, and liver lesions); at 60 mg/kg (scarring on the spleen, irregularly shaped or adhesions on livers, irregular pigmentation of kidney, heart enlargement, and fluid in cranial cavity); at 125 mg/kg (tan lungs, red fluid in cranial cavity, and pigmentation of testicle); at 250 mg/kg (splenic enlargement and red fluid in cranial cavity); and at 500 mg/kg (tan-dark lung, fluid in abdominal cavity, and red fluid in cranial cavity).

Gross lesions observed in the WR269410-treated females included: at 30 mg/kg (scarring of kidney, scarring and enlargement of spleen, and liver adhesions and deformities); at 60 mg/kg (irregular pigmentation of kidney, scarring and enlargement of spleen, enlargement of heart, fluid in cranial cavity, and liver adhesions and deformities); at 125 mg/kg (tan lungs and red fluid in cranial cavity); at 250 mg/kg (tan-dark lung, red fluid in cranial cavity, and fluid in abdominal cavity); and at 500 mg/kg (tan-dark lung, fluid in abdominal cavity, and red fluid in cranial cavity).

4.2B.2.5 Mortality

The dose-mortality data are shown in Table 9. The intraperitoneal LD50 of WR26941 for male rats is 155 mg/kg with a 95% confidence interval of 59 to 408 mg/kg. The dose-mortality curve slope (probit/log dose) is 2.08. (Appendix 6). For female rats, an intraperitoneal LD50 was estimated from log-probability paper to be approximately 70 - 80 mg/kg. This could not be further defined as the incidence of mortality at two juxtaposed dose levels, 43 and 134 mg/kg, were 0% and 100%, respectively.

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5.0 DISCUSSION/CONCLUSION

This study determined and compared the acute oral and intraperitoneal toxicity of WR242511 tartrate and WR269410 in male and female rats. The oral LD50 of WR242511 tartrate for male rats was 16.3 mg base/kg with a 95% confidence interval of 13.8 to 19.4 mg base/kg and the dose-mortality curve slope (probit/log dose) was 8.27. The calculated LD50 for female rats was 135 mg base/kg with a 95% confidence interval of 77 to 236 mg base/kg and the dose-mortality curve slope (probit/log dose) was 3.58. The data show that the LD50 value for males is approximately eight-fold lower than for female rats. Thus, a significant sex difference exists in the acute oral toxicity of WR242511 tartrate.

The calculated intraperitoneal LD50 of WR242511 tartrate in males was 23 mg base/kg with a 95% confidence interval of 14 to 37 mg base/kg and the dose-mortality curve slope (probit/log dose) was 2.68. In females, the LD50 was 30 mg base/kg with a 95% confidence interval of 14 to 66 mg base/kg and the dose-mortality curve slope (probit/log dose) was 1.49. Because of the similarity of the LD50 values, and the overlap of the 95% confidence intervals, no significant difference exists between the sexes in the acute intraperitoneal toxicity of WR242511 tartrate. Further, the LD50 values obtained from both sexes for the intraperitoneal administration of WR242511 tartrate were not significantly different from the LD50 value from males given the test article orally. However, female rats appear significantly less sensitive to the acute oral toxicity of WR242511 tartrate compared to intraperitoneal administration.

In the oral acute toxicity test of WR269410, the oral LD50 for male rats was 420 mg/kg with a 95% confidence interval of 219 to 806 mg/kg and the dose-mortality curve slope (probit/log dose) was 1.54. The calculated LD50 for female rats was 147 mg/kg with a 95% confidence interval of 70 to 310 mg/kg and the dose-mortality curve slope (probit/log dose) was 1.44. Based on these results, female rats appear to be moderately more sensitive to oral WR269410 administration than males. Although slight overlap of the two 95% confidence limits occurred, the LD50 in males was about three times higher than in females.

In the initial range-finding tests, WR269410 was administered in 0.1% Methylcellulose/0.4% Tween 80. Due to the physical inability to intraperitoneally administer WR269410 dosage formulations at high enough concentrations to produce lethality, WR269410 was subsequently administered intraperitoneally as a solution in polyethylene glycol 200 (PEG 200) after consultation with the Sponsor. From the results of the toxicity test, the calculated intraperitoneal LD50 of WR269410 in males was 156 mg/kg with a 95% confidence interval of 59 to 408 mg/kg and a dose-mortality curve slope (probit/log dose) was 2.08. An LD50 value was estimated in females to be apparently 70 - 80 mg/kg. These data obtained in this study suggest that WR242511 tartrate is more toxic than WR269410 when administered orally. Based on the oral LD50 data and after consultation with the Sponsor, the following dose levels are suggested to be used in the two week oral dose range-finding studies in rats of WR242511 tartrate; 0, 0.5, 2.0, and 6.2 mg base/kg/day, and of WR269410; 0, 2.0, 6.0, 18.0 mg/kg/day.

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6.0 PERSONNEL:

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Quality Assurance	Ronald C. Schoenbeck

Report preparation was assisted by Clyde W. Wheeler, Ph.D. and Teresa O'Neill, B.S..

7.0 ARCHIVES

The raw data, test article reserve sample and final report are archived at the Toxicology Research Laboratory (TRL), University of Illinois at Chicago (UIC), Department of Pharmacology, 1940 W. Taylor St., Chicago, IL 60612-7353.

8.0 REFERENCE

Litchfield, J.T. and Wilcoxon, F. (1949). A simplified method of evaluating dose-effect experiments. *J. Pharmacol. Exp. Ther.* 96, 99-115.

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Table 1

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

Calculated LD50 Values

WR242511 Tartrate

Route	Sex	LD50 (mg base/kg)	95% Confidence Interval (mg base/kg)	Dose- Mortality Curve Slope (probit/log dose)
Oral	Male	16.3	13.8 - 19.4	8.27
	Female	135	77 - 236	3.58
Intraperitoneal	Male	23 ² / ₃	14 - 37	2.68
	Female	30	14 - 66	1.49

WR269410

Route	Sex	LD50 (mg/kg)	95% Confidence Interval (mg/kg)	Dose-Mortality Curve Slope (probit/log dose)
Oral	Male	420 ² / ₃	219 - 806	1.54
	Female	147	70 - 310	1.44
Intraperitoneal	Male	155	59 - 408	2.08
	Female	70 - 80(est.)	--	--

Table 2

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATSDosage Formulation Analysis^a*WR242511 Tartrate (Gavage)*

Target Concentration (mg base/ml)	Actual Concentration (mg base/ml) ^b	% Target
2.0	1.90 ± 0.0078	95.0
3.0	2.74 ± 0.0023	91.3
4.0	3.97 ± 0.0077	99.2
5.0	4.58 ± 0.0124	91.6
7.0	6.41 ± 0.0109	91.5
10	9.71 ± 0.0889	97.1
22	21.50 ± 0.1055	97.7
50	49.59 ± 0.1897	99.2
120	123.67 ± 0.4024	101.4

WR242511 Tartrate (Intraperitoneal)

Target Concentration (mg base/ml)	Actual Concentration (mg base/ml) ^b	% Target
1.0	1.00 ± 0.0039	100.0
2.0	1.94 ± 0.0139	97.0
3.3	3.29 ± 0.0241	99.7
4.0	3.97 ± 0.0077	99.2
6.0	6.37 ± 0.0770	106.2
10	9.71 ± 0.0889	97.1
22	21.50 ± 0.1055	97.7
50	49.59 ± 0.1897	99.2
120	123.67 ± 0.4024	101.4

^aMean ± standard deviation for triplicate runs.^bThe samples were assayed within 24 hours prior to use on Day 0.

Table 2 (contd.)

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATSDosage Formulation Analysis^a*WR269410 (Gavage)*

Target Concentration (mg/ml)	Actual Concentration (mg/ml) ^b	% Target
2.0	2.13 \pm 0.0034	106.5
4.0	4.30 \pm 0.0601	107.5
7.5	7.82 \pm 0.0264	104.3
7.5	8.08 \pm 0.1122	107.7
11.5	11.46 \pm 0.0310	99.7
17.5	19.03 \pm 0.1575	108.7
27.5	26.70 \pm 0.2284	97.1
35.0	34.91 \pm 0.2858	99.7
45.0	47.34 \pm 0.1992	105.2
57.5	61.53 \pm 0.1389	107.0
75.0	71.45 \pm 0.2701	95.3

WR269410 (Intraperitoneal)

Target Concentration (mg/ml)	Actual Concentration (mg/ml) ^b	% Target	Dose Level Administered (mg/kg)
6.0	6.9	115.0	35
12	8.5	70.8	43
25	26.7	106.8	134
50	42.9	85.8	215
100	94.5	94.5	473

^aMean \pm standard deviation for triplicate runs.^bThe samples were assayed within 24 hours prior to use on Day 0.

Table 3.1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104P024

SEX: MALE

DOSE:(mg/kg) GROUP:	10 1-M	15 2-M	20 3-M	25 4-M	35 5-M	50 6-M	110 7-M	250 8-M
Scheduled Sacrifice	5	5	0	0	0	0	0	0
Animal Found Dead	0	0	5	5	5	5	0	0
Decreased Activity	0	0	3	2	4	4	0	0
Ataxia	0	0	0	0	0	1	0	0
Dark Material Around Nose	0	0	0	0	1	0	0	0
Hunched Posture	1	4	0	0	3	5	0	0
Labored Breathing	0	0	0	0	1	0	0	0
Lethargic	0	0	0	0	1	0	0	0
Rough Coat	5	5	5	5	5	5	0	0
Rough Coat 1	0	0	0	0	2	2	0	0
Rough Coat 2	2	2	1	1	4	2	0	0
Rough Coat 3	5	5	5	5	5	5	0	0
Hunched Posture 3	0	0	0	0	1	2	0	0
Total Number of Animals	5	5	5	5	5	5	0	0

Table 3.1 (Continued)

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104P024

SEX: MALE

DOSE:(mg/kg) 600
GROUP: 9-M

Scheduled Sacrifice	0
Animal Found Dead	0
Decreased Activity	0
Ataxia	0
Dark Material Around Nose	0
Hunched Posture	0
Labored Breathing	0
Lethargic	0
Rough Coat	0
Rough Coat 1	0
Rough Coat 2	0
Rough Coat 3	0
Hunched Posture 3	0
Total Number of Animals	0

Table 3.2

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104PO4A

SEX: MALE

	DOSE:(mg/kg)	16.5	18.0
	GROUP:	1-M	2-M
Scheduled Sacrifice		2	1
Animal Found Dead		3	4
Activity Decreased		1	3
Hunched Posture		5	5
Rough Coat		5	5
Hunched Posture 2		3	5
Hunched Posture 3		5	5
Rough Coat 1		3	1
Rough Coat 2		5	5
Rough Coat 3		5	5
Total Number of Animals		5	5

Table 3.3

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104IP24

SEX: MALE

DOSE:(mg/kg) GROUP:	20 1-M	50 2-M	110 3-M	250 4-M	600 5-M
Scheduled Sacrifice	1	0	0	1	0
Animal Found Dead	4	5	5	4	5
Decreased Activity	4	1	0	1	0
Dark Material Around Eyes	2	0	0	0	0
Dark Material Around Nose	3	0	0	1	0
Hunched Posture	5	3	0	1	0
Labored Breathing	1	0	0	0	0
Lethargic	1	0	0	0	0
Rough Coat	5	3	0	1	0
Rough Coat 1	5	5	5	5	5
Rough Coat 2	5	5	3	2	3
Rough Coat 3	5	5	1	1	2
Decreased Activity 1	5	3	5	4	0
Decreased Activity 2	3	0	2	1	3
Decreased Activity 3	3	5	1	1	2
Hunched Posture 1	0	0	5	5	0
Hunched Posture 2	5	5	3	2	3
Hunched Posture 3	5	5	1	1	1
Blue Feet 2	0	3	2	1	3
Blue Feet 3	0	2	0	0	0
Abdomen Bloated	1	0	0	1	0
Abdomenal Lesion	0	0	0	1	0
Lethargic 2	0	0	0	1	0
Total Number of Animals	5	5	5	5	5

Table 3.4

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104IP4A

SEX: MALE

DOSE:(mg/kg) GROUP:	5 1-M	10 2-M	16.5 3-M	30 4-M
Scheduled Sacrifice	5	5	4	2
Animal Found Dead	0	0	1	3
Activity Decreased	1	4	5	4
Dark Material Around Eyes	0	0	0	1
Dark Material Around Nose	0	1	4	1
Hunched Posture	5	5	5	5
Rough Coat	5	5	5	5
Hunched Posture 1	1	3	5	5
Hunched Posture 2	4	5	5	5
Hunched Posture 3	5	5	5	5
Rough Coat 1	3	5	5	4
Rough Coat 2	5	5	5	5
Rough Coat 3	5	5	5	5
Abdomen Bloated	0	1	5	3
Total Number of Animals	5	5	5	5

Table 3.5

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104PO26

SEX: MALE

DOSE:(mg/kg) GROUP:	550 1-M	700 2-M	900 3-M	1150 4-M	1500 5-M
Scheduled Sacrifice	3	3	1	2	0
Animal Found Dead	2	2	4	3	5
Decreased Activity	4	4	2	2	1
Ataxia	0	0	1	1	4
Comatose	2	0	1	0	0
Dark Material Around Eyes	0	0	1	0	0
Dark Material Around Nose	0	0	1	0	1
Hunched Posture	3	4	1	2	1
Labored Breathing	0	1	2	1	3
Lethargic	0	1	0	0	0
Rough Coat	5	5	3	3	4
Rough Coat 1	5	5	5	5	5
Rough Coat 2	5	5	5	5	5
Rough Coat 3	5	5	5	5	5
Blue Feet	5	5	3	3	4
Blue Feet 1	5	5	5	5	5
Blue Feet 2	5	5	5	5	5
Blue Feet 3	5	5	5	5	5
Hunched Posture 1	0	1	0	0	0
Hunched Posture 2	0	1	0	0	0
Hunched Posture 3	2	1	0	0	0
Decreased Activity 1	3	1	0	0	0
Decreased Activity 2	1	2	0	0	0
Decreased Activity 3	2	1	0	0	0
Comatose 1	1	2	4	2	1
Comatose 2	2	2	4	4	2
Comatose 3	2	1	4	4	3
Lethargic 1	1	2	1	3	4
Lethargic 2	2	1	1	1	3
Lethargic 3	1	3	1	1	2
Ataxia 1	0	0	1	0	0
Ataxia 2	0	0	0	1	0
Labored Breathing 1	2	3	5	4	5
Labored Breathing 2	0	3	5	4	5
Labored Breathing 3	3	4	5	4	5
Total Number of Animals	5	5	5	5	5

Table 3.6

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104PO6A

SEX: MALE

DOSE:(mg/kg) GROUP:	150 1-M	230 2-M	350 3-M
Scheduled Sacrifice	0	3	1
Animal Found Dead	0	2	4
Activity Decreased	0	4	2
Ataxia	0	1	1
Dark Material Around Eyes	0	1	1
Hunched Posture	0	3	1
Rough Coat	0	4	2
Activity Decreased 1	0	5	3
Activity Decreased 2	0	5	2
Activity Decreased 3	0	4	2
Hunched Posture 1	0	4	1
Hunched Posture 2	0	3	2
Hunched Posture 3	0	2	1
Rough Coat 1	0	2	4
Rough Coat 2	0	3	1
Rough Coat 3	0	5	4
Comatose 1	0	0	1
Comatose 2	0	0	2
Comatose 3	0	1	2
Blue Feet	0	4	2
Blue Feet 1	0	5	4
Blue Feet 2	0	5	4
Blue Feet 3	0	5	4
Blue Tail	0	2	0
Total Number of Animals	0	5	5

Table 3.7

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104PO6B

SEX: MALE

DOSE:(mg/kg) GROUP:	40 1-M	80 2-M	150 3-M
Scheduled Sacrifice	5	5	5
Decreased Activity	0	1	0
Hunched Posture	5	5	5
Rough Coat	5	5	5
Blue Feet	0	3	5
Rough Coat 1	5	5	5
Rough Coat 2	5	5	5
Rough Coat 3	5	5	5
Blue Feet 1	3	5	5
Blue Feet 2	3	5	5
Blue Feet 3	5	5	5
Decreased Activity	0	4	5
Decreased Activity	0	4	5
Decreased Activity	0	3	5
Hunched Posture 1	4	5	5
Hunched Posture 2	5	4	5
Hunched Posture 3	5	5	5
Labored Breathing 3	0	1	0
Blue Tail	0	0	1
Total Number of Animals	5	5	5

Table 3.8

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104IP26

SEX: MALE

DOSE:(mg/kg) GROUP:	30 1-M	60 2-M	125 3-M	250 4-M	500 5-M
Scheduled Sacrifice	5	5	2	2	1
Animal Found Dead	0	0	3	3	4
Decreased Activity	1	4	2	2	1
Dark Material Around Nose	1	0	0	0	0
Hunched Posture	5	5	3	2	1
Lethargic	0	0	1	0	1
Rough Coat	5	5	3	2	1
Blue Feet	0	0	1	1	1
Hunched Posture #1	3	0	0	2	2
Hunched Posture #2	4	4	2	2	1
Hunched Posture #3	5	5	2	2	1
Decreased Activity #1	1	2	2	2	2
Decreased Activity #2	2	0	0	2	0
Decreased Activity #3	4	3	2	2	0
Rough Coat #1	2	5	4	5	5
Rough Coat #2	4	5	5	5	3
Rough Coat #3	5	5	5	5	3
Blue Feet #1	5	5	5	5	5
Blue Feet #2	5	5	5	5	3
Blue Feet #3	5	5	5	5	3
Lethargic #1	4	3	1	0	0
Lethargic #2	3	5	2	0	1
Lethargic #3	1	2	1	0	1
Labored Breathing #1	0	0	3	3	3
Labored Breathing #2	0	0	3	3	2
Labored Breathing #3	0	0	3	3	3
Comatose #1	0	0	2	3	3
Comatose #2	0	0	3	3	2
Comatose #3	0	0	2	3	2
Total Number of Animals	5	5	5	5	5

Table 4.1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104P024

SEX: FEMALE

DOSE:(mg/kg) GROUP:	10 1-F	15 2-F	20 3-F	25 4-F	35 5-F	50 6-F	110 7-F	250 8-F
Scheduled Sacrifice	0	0	5	0	0	5	3	1
Animal Found Dead	0	0	0	0	0	0	2	4
Decreased Activity	0	0	0	0	0	0	4	2
Ataxia	0	0	0	0	0	0	0	1
Dark Material Around Eyes	0	0	0	0	0	0	0	2
Dark Material Around Nose	0	0	0	0	0	0	0	1
Hunched Posture	0	0	0	0	0	4	5	5
Labored Breathing	0	0	0	0	0	0	0	1
Rough Coat	0	0	5	0	0	5	5	5
Rough Coat 2	0	0	0	0	0	0	2	5
Rough Coat 3	0	0	2	0	0	5	4	5
Hunched Posture2	0	0	0	0	0	0	0	0
Hunched Posture 3	0	0	0	0	0	2	1	5
Decreased Activity 2	0	0	0	0	0	0	0	0
Decreased Activity 3	0	0	0	0	0	0	0	1
Total Number of Animals	0	0	5	0	0	5	5	5

Table 4.1 (Continued)
ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104P024

SEX: FEMALE

DOSE:(mg/kg) 600
GROUP: 9-F

Scheduled Sacrifice	0
Animal Found Dead	5
Decreased Activity	2
Ataxia	0
Dark Material Around Eyes	0
Dark Material Around Nose	0
Hunched Posture	2
Labored Breathing	0
Rough Coat	2
Rough Coat 2	5
Rough Coat 3	5
Hunched Posture2	4
Hunched Posture 3	5
Decreased Activity 2	2
Decreased Activity 3	0
Total Number of Animals	5

Table 4.2

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104IP24

SEX: FEMALE

DOSE:(mg/kg) GROUP:	20 1-F	50 2-F	110 3-F	250 4-F	600 5-F
Scheduled Sacrifice	2	0	0	0	0
Animal Found Dead	3	5	5	5	5
Decreased Activity	0	1	1	0	0
Dark Material Around Nose	2	2	0	0	0
Hunched Posture	5	5	1	0	0
Lethargic	1	1	0	0	0
Rough Coat	5	5	1	0	0
Rough Coat 1	5	5	5	1	5
Rough Coat 2	5	5	2	0	1
Rough Coat 3	5	5	2	0	0
Decreased Activity 1	0	5	4	0	3
Decreased Activity 2	0	3	0	0	0
Decreased Activity 3	0	3	1	0	0
Hunched Posture 1	2	5	5	1	0
Hunched Posture 2	5	5	1	0	1
Hunched Posture 3	5	5	2	0	0
Blue Feet 1	0	0	0	1	0
Blue Feet 2	0	5	1	0	1
Blue Feet 3	0	2	2	0	0
Abdomen Bloated	4	4	0	0	0
Lethargic 1	0	0	0	1	0
Lethargic 2	0	0	1	0	1
Lethargic 3	0	0	1	0	0
Total Number of Animals	5	5	5	5	5

Table 4.3

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104IP4A

SEX: FEMALE

DOSE:(mg/kg) GROUP:	5 1-F	10 2-F	16.5 3-F	30 4-F
Scheduled Sacrifice	5	5	5	2
Animal Found Dead	0	0	0	3
Activity Decreased	3	4	3	3
Hunched Posture	5	5	5	5
Rough Coat	5	5	5	5
Activity Decreased 1	0	0	0	1
Activity Decreased 2	0	0	0	1
Hunched Posture 1	0	5	5	5
Hunched Posture 2	5	5	5	5
Hunched Posture 3	5	5	5	5
Rough Coat 1	0	2	5	5
Rough Coat 2	1	5	5	5
Rough Coat 3	5	5	5	5
Blue Feet	0	0	0	2
Abdomen Bloated	0	0	3	4
Total Number of Animals	5	5	5	5

Table 4.4

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104PO26

SEX: FEMALE

DOSE:(mg/kg) GROUP:	550 1-F	700 2-F	900 3-F	1150 4-F	1500 5-F
Scheduled Sacrifice	1	1	0	2	0
Animal Found Dead	4	4	5	3	5
Decreased Activity	1	1	0	4	1
Ataxia	0	0	0	1	1
Comatose	1	0	0	1	1
Dark Material Around Eyes	0	0	0	1	0
Hunched Posture	1	1	0	4	1
Labored Breathing	1	0	0	1	1
Rough Coat	2	1	0	5	2
First Clinical Sign	1	0	1	0	2
Second Clinical Sign	0	1	1	0	0
Third Clinical Sign	1	1	1	0	0
Rough Coat 1	4	5	4	4	3
Rough Coat 2	4	4	3	5	3
Rough Coat 3	3	3	2	5	3
Blue Feet	2	1	0	5	2
Blue Feet 1	4	5	4	5	3
Blue Feet 2	4	4	3	5	3
Blue Feet 3	3	3	2	5	3
Hunched Posture 1	0	1	0	2	0
Hunched Posture 2	1	1	0	2	0
Hunched Posture 3	1	1	0	2	0
Decreased Activity 1	0	1	0	2	0
Decreased Activity 2	0	1	0	0	0
Decreased Activity 3	1	0	0	3	0
Comatose 1	3	4	4	1	1
Comatose 2	2	3	3	2	2
Comatose 3	2	2	2	1	2
Lethargic 1	1	0	0	2	2
Lethargic 2	2	0	0	3	1
Lethargic 3	0	1	0	1	1
Ataxia 2	0	0	0	2	0
Ataxia 3	1	0	0	2	0
Labored Breathing 1	3	4	4	2	3
Labored Breathing 2	3	3	3	3	3
Labored Breathing 3	2	2	2	3	2
Tip of Tail Darkened	0	0	0	3	0
End Half of Tail Darkened	0	0	0	1	0
Total Number of Animals	5	5	5	5	5

Table 4.5

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104PO6A

SEX: FEMALE

DOSE:(mg/kg) GROUP:	150 1-F	230 2-F	350 3-F
Scheduled Sacrifice	3	0	1
Animal Found Dead	2	5	4
Activity Decreased	4	0	1
Comatose	1	0	0
Hunched Posture	3	0	1
Labored Breathing	1	0	0
Rough Coat	4	0	1
Activity Decreased 1	4	1	1
Activity Decreased 2	4	0	1
Activity Decreased 3	4	0	1
Hunched Posture 1	4	0	1
Hunched Posture 2	4	0	1
Hunched Posture 3	4	0	1
Rough Coat 1	1	2	3
Rough Coat 2	4	1	3
Rough Coat 3	3	3	3
Comatose 1	0	4	3
Comatose 2	0	4	2
Comatose 3	0	4	2
Blue Feet	3	0	1
Blue Feet 1	4	5	4
Blue Feet 2	4	4	3
Blue Feet 3	3	4	3
Blue Tail	1	0	1
Total Number of Animals	5	5	5

Table 4.6

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104PO6B

SEX: FEMALE

DOSE:(mg/kg) GROUP:	40 1-F	80 2-F	150 3-F
Scheduled Sacrifice	5	5	0
Decreased Activity	0	2	0
Hunched Posture	5	5	0
Rough Coat	5	5	0
Blue Feet	1	5	0
Rough Coat 1	5	5	0
Rough Coat 2	5	5	0
Rough Coat 3	5	5	0
Blue Feet 1	5	5	0
Blue Feet 2	5	5	0
Blue Feet 3	5	5	0
Decreased Activity	0	5	0
Decreased Activity	0	4	0
Decreased Activity	0	5	0
Hunched Posture 1	5	5	0
Hunched Posture 2	5	5	0
Hunched Posture 3	5	5	0
Blue Tail	0	2	0
Total Number of Animals	5	5	0

Table 4.7

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF CLINICAL SIGNS

STUDY: 104IP26

SEX: FEMALE

DOSE:(mg/kg) GROUP:	30 1-F	60 2-F	125 3-F	250 4-F	500 5-F
Scheduled Sacrifice	5	5	0	0	0
Animal Found Dead	0	0	5	5	5
Comatose	0	0	1	0	0
Decreased Activity	0	4	0	0	0
Hunched Posture	5	5	0	0	0
Labored Breathing	0	0	1	0	0
Rough Coat	5	5	1	0	0
Blue Feet	2	0	1	0	0
Hunched Posture #1	0	0	0	0	1
Hunched Posture #2	5	4	0	0	1
Hunched Posture #3	5	5	0	0	0
Decreased Activity #1	1	1	0	0	0
Decreased Activity #2	1	0	0	0	0
Decreased Activity #3	4	2	0	0	0
Rough Coat #1	4	5	5	5	5
Rough Coat #2	5	5	5	4	2
Rough Coat #3	5	5	5	4	2
Blue Feet #1	5	5	5	5	5
Blue Feet #2	5	5	5	4	2
Blue Feet #3	5	5	5	4	2
Lethargic #1	4	4	0	0	1
Lethargic #2	4	5	0	0	0
Lethargic #3	1	3	0	0	0
Labored Breathing #1	0	0	5	5	4
Labored Breathing #2	0	0	5	4	2
Labored Breathing #3	0	0	5	4	2
Comatose #1	0	0	5	5	4
Comatose #2	0	0	5	4	2
Comatose #3	0	0	5	4	2
Total Number of Animals	5	5	5	5	5

Table 5.1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104P024

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	10 1-M	15 2-M	20 3-M	25 4-M	35 5-M	50 6-M	110 7-M	250 8-M
DAY -3	MEAN	280.2	274.7	280.5	278.8	280.4	279.2	--	--
	S.D.	14.27	12.51	17.45	12.47	14.49	10.78	--	--
	N	5	5	5	5	5	5	0	0
DAY 0	MEAN	275.2	273.8	279.7	278.6	280.5	277.9	--	--
	S.D.	17.50	9.48	19.86	13.18	13.05	12.69	--	--
	N	5	5	5	5	5	5	0	0
DAY 7	MEAN	334.1	328.4	--	--	--	--	--	--
	S.D.	30.21	26.41	--	--	--	--	--	--
	N	5	5	0	0	0	0	0	0
DAY 14	MEAN	367.6	392.2	--	--	--	--	--	--
	S.D.	53.32	57.23	--	--	--	--	--	--
	N	5	5	0	0	0	0	0	0

-- = Data Unavailable

Table 5.1 (Continued)
 ACUTE ORAL TOXICITY STUDY
 OF WR242511 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104P024

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	600 9-M
DAY -3	MEAN	--
	S.D.	--
	N	0
DAY 0	MEAN	--
	S.D.	--
	N	0
DAY 7	MEAN	--
	S.D.	--
	N	0
DAY 14	MEAN	--
	S.D.	--
	N	0

Table 5.2

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104PO4A

SEX: MALE

PERIOD		DOSE: (mg/kg)	16.5	18.0
		GROUP:	1-M	2-M
DAY -2	MEAN		359.8	363.7
	S.D.		21.80	27.93
	N		5	5
DAY 0	MEAN		339.3	341.0
	S.D.		18.10	26.98
	N		5	5
DAY 7	MEAN		335.7	390.8
	S.D.		14.35	0.00
	N		2	1
DAY 14	MEAN		386.3	438.4
	S.D.		13.93	0.00
	N		2	1

Table 5.3

**ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS**

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104IP24

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	20 1-M	50 2-M	110 3-M	250 4-M	600 5-M
DAY -3	MEAN	278.7	280.7	278.7	278.6	277.9
	S.D.	12.77	13.85	12.63	13.94	12.59
	N	5	5	5	5	5
DAY 0	MEAN	305.9	303.4	301.6	300.9	304.1
	S.D.	15.01	14.69	13.12	17.13	14.94
	N	5	5	5	5	5
DAY 7	MEAN	291.8	--	--	298.4	--
	S.D.	0.00	--	--	0.00	--
	N	1	0	0	1	0
DAY 14	MEAN	352.8	--	--	348.2	--
	S.D.	0.00	--	--	0.00	--
	N	1	0	0	1	0

Table 5.4

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104IP4A

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	5	10	16.5	30
		1-M	2-M	3-M	4-M
DAY -2	MEAN	364.1	362.9	365.9	362.8
	S.D.	28.60	22.77	25.40	24.75
	N	5	5	5	5
DAY 0	MEAN	360.6	371.8	374.3	366.8
	S.D.	30.45	21.41	28.99	25.77
	N	5	5	5	5
DAY 7	MEAN	397.0	410.5	369.9	390.7
	S.D.	35.31	25.13	20.31	9.47
	N	5	5	5	2
DAY 14	MEAN	436.0	445.9	407.1	445.5
	S.D.	42.88	20.50	31.69	4.17
	N	5	5	4	2

Table 5.5

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104P026

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	550 1-M	700 2-M	900 3-M	1150 4-M	1500 5-M
DAY -4	MEAN	281.5	276.0	279.9	281.2	279.9
	S.D.	12.82	16.04	10.46	14.22	17.95
	N	5	5	5	5	5
DAY 0	MEAN	288.2	283.2	286.1	289.6	287.8
	S.D.	9.57	20.28	24.18	15.95	19.75
	N	5	5	5	5	5
DAY 7	MEAN	319.5	307.9	278.7	270.1	--
	S.D.	16.86	26.48	0.00	5.73	--
	N	3	3	1	2	0
DAY 14	MEAN	388.5	375.6	392.6	355.1	--
	S.D.	16.60	32.25	0.00	21.07	--
	N	3	3	1	2	0

Table 5.6

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104PO6A

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	150	230	350
		1-M	2-M	3-M
DAY -2	MEAN	--	363.1	353.7
	S.D.	--	17.88	26.19
	N	0	5	5
DAY 7	MEAN	--	356.9	412.5
	S.D.	--	48.99	0.00
	N	0	3	1
DAY 14	MEAN	--	426.2	468.1
	S.D.	--	43.61	0.00
	N	0	3	1

Table 5.7

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104PO6B

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	40 1-M	80 2-M	150 3-M
DAY -3	MEAN	185.2	186.1	186.2
	S.D.	8.99	12.09	9.69
	N	5	5	5
DAY 0	MEAN	196.8	200.1	194.6
	S.D.	8.17	14.75	8.34
	N	5	5	5
DAY 7	MEAN	277.5	269.6	268.0
	S.D.	7.47	13.63	6.50
	N	5	5	5
DAY 14	MEAN	348.8	335.0	329.3
	S.D.	10.78	25.51	15.77
	N	5	5	5

Table 5.8

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104IP26

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	30 1-M	60 2-M	125 3-M	250 4-M	500 5-M
DAY -3	MEAN	256.4	258.4	256.8	253.3	257.9
	S.D.	14.25	15.65	11.24	15.38	11.13
	N	5	5	5	5	5
DAY 0	MEAN	275.9	276.9	277.1	271.2	275.8
	S.D.	13.95	15.63	13.42	13.15	9.18
	N	5	5	5	5	5
DAY 7	MEAN	311.6	302.9	321.9	306.0	316.3
	S.D.	23.54	18.18	32.46	12.80	0.00
	N	5	5	2	2	1
DAY 14	MEAN	362.7	351.5	363.1	360.2	381.5
	S.D.	34.47	23.38	35.78	23.41	0.00
	N	5	5	2	2	1

Table 6.1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104P024

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	10 1-M	15 2-M	20 3-M	25 4-M	35 5-M	50 6-M	110 7-M	250 8-M
DAY 7	MEAN	58.9	54.6	--	--	--	--	--	--
	S.D.	14.74	21.66	--	--	--	--	--	--
	N	5	5	0	0	0	0	0	0
DAY 14	MEAN	33.5	63.8	--	--	--	--	--	--
	S.D.	26.50	40.23	--	--	--	--	--	--
	N	5	5	0	0	0	0	0	0
TOTAL GAIN	MEAN	92.4	118.4	--	--	--	--	--	--
	S.D.	40.69	52.80	--	--	--	--	--	--
	N	5	5	0	0	0	0	0	0

-- = Data Unavailable

Table 6.1 (Continued)
 ACUTE ORAL TOXICITY STUDY
 OF WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104P024

SEX: MALE

PERIOD	DOSE: (mg/kg)	600
	GROUP:	9-M
DAY 7	MEAN	--
	S.D.	--
	N	0
DAY 14	MEAN	--
	S.D.	--
	N	0
TOTAL GAIN	MEAN	--
	S.D.	--
	N	0

Table 6.2

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104PO4A

SEX: MALE

PERIOD		DOSE: (mg/kg)	16.5	18.0
		GROUP:	1-M	2-M
DAY 7	MEAN		13.8	52.5
	S.D.		7.71	0.00
	N		2	1
DAY 14	MEAN		50.6	47.6
	S.D.		0.42	0.00
	N		2	1
TOTAL GAIN	MEAN		64.4	100.1
	S.D.		7.28	0.00
	N		2	1

Table 6.3

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104IP24

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	20 1-M	50 2-M	110 3-M	250 4-M	600 5-M
DAY 7	MEAN	-36.9	--	--	-10.7	--
	S.D.	0.00	--	--	0.00	--
	N	1	0	0	1	0
DAY 14	MEAN	61.0	--	--	49.8	--
	S.D.	0.00	--	--	0.00	--
	N	1	0	0	1	0
TOTAL GAIN	MEAN	24.1	--	--	39.1	--
	S.D.	0.00	--	--	0.00	--
	N	1	0	0	1	0

Table 6.4

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104IP4A

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	5 1-M	10 2-M	16.5 3-M	30 4-M
DAY 7	MEAN	36.4	38.8	-4.4	-0.6
	S.D.	7.76	4.99	36.70	5.52
	N	5	5	5	2
DAY 14	MEAN	39.0	35.4	37.0	54.8
	S.D.	8.81	7.86	13.76	5.30
	N	5	5	4	2
TOTAL GAIN	MEAN	75.4	74.1	44.1	54.2
	S.D.	13.73	5.56	42.11	0.21
	N	5	5	4	2

Table 6.5
ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104PO26

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	550 1-M	700 2-M	900 3-M	1150 4-M	1500 5-M
DAY 7	MEAN	30.0	25.7	-25.7	-12.0	--
	S.D.	6.19	2.27	0.00	15.20	--
	N	3	3	1	2	0
DAY 14	MEAN	69.0	67.7	113.9	85.1	--
	S.D.	1.46	5.80	0.00	15.34	--
	N	3	3	1	2	0
TOTAL GAIN	MEAN	99.0	93.4	88.2	73.1	--
	S.D.	7.07	5.88	0.00	0.14	--
	N	3	3	1	2	0

Table 6.6
ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104PO6A

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	150 1-M	230 2-M	350 3-M
DAY 7	MEAN	--	10.4	48.0
	S.D.	--	29.40	0.00
	N	0	3	1
DAY 14	MEAN	--	69.3	55.6
	S.D.	--	7.30	0.00
	N	0	3	1
TOTAL GAIN	MEAN	--	79.7	103.6
	S.D.	--	22.56	0.00
	N	0	3	1

Table 6.7

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104PO6B

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	40	80	150
		1-M	2-M	3-M
DAY 7	MEAN	80.7	69.5	73.4
	S.D.	5.30	13.98	11.14
	N	5	5	5
DAY 14	MEAN	71.3	65.4	61.3
	S.D.	7.14	17.65	9.75
	N	5	5	5
TOTAL GAIN	MEAN	152.0	134.9	134.7
	S.D.	11.93	31.47	19.98
	N	5	5	5

Table 6.8

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104IP26

SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	30 1-M	60 2-M	125 3-M	250 4-M	500 5-M
DAY 7	MEAN	35.7	26.1	39.9	45.7	39.7
	S.D.	18.73	9.81	15.63	0.71	0.00
	N	5	5	2	2	1
DAY 14	MEAN	51.1	48.6	41.3	54.2	65.2
	S.D.	15.25	8.37	3.32	10.61	0.00
	N	5	5	2	2	1
TOTAL GAIN	MEAN	86.8	74.7	81.1	99.9	104.9
	S.D.	27.68	14.62	18.95	9.90	0.00
	N	5	5	2	2	1

Table 7.1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104P024

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	10 1-F	15 2-F	20 3-F	25 4-F	35 5-F	50 6-F	110 7-F	250 8-F
DAY -3	MEAN	--	--	204.4	--	--	205.0	202.7	204.1
	S.D.	--	--	13.57	--	--	12.46	13.30	11.29
	N	0	0	5	0	0	5	5	5
DAY 0	MEAN	--	--	198.6	--	--	200.3	194.9	199.2
	S.D.	--	--	12.12	--	--	9.78	11.55	9.56
	N	0	0	5	0	0	5	5	5
DAY 7	MEAN	--	--	225.0	--	--	221.9	189.3	155.7
	S.D.	--	--	16.48	--	--	15.87	31.21	0.00
	N	0	0	5	0	0	5	4	1
DAY 14	MEAN	--	--	269.8	--	--	237.3	239.4	198.4
	S.D.	--	--	50.04	--	--	21.81	11.15	0.00
	N	0	0	5	0	0	5	3	1

-- = Data Unavailable

Table 7.1 (continued)
ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104P024

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	600 9-F
DAY -3	MEAN S.D. N	206.6 13.72 5
DAY 0	MEAN S.D. N	202.7 9.43 5
DAY 7	MEAN S.D. N	-- -- 0
DAY 14	MEAN S.D. N	-- -- 0

-- = Data Unavailable

Table 7.2

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104IP24

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	20 1-F	50 2-F	110 3-F	250 4-F	600 5-F
DAY -3	MEAN	203.5	202.8	202.6	204.6	202.4
	S.D.	11.58	14.83	15.09	13.17	10.84
	N	5	5	5	5	5
DAY 0	MEAN	216.7	212.4	211.2	214.8	210.7
	S.D.	11.86	12.61	17.29	16.88	10.12
	N	5	5	5	5	5
DAY 7	MEAN	216.8	--	--	--	--
	S.D.	2.12	--	--	--	--
	N	2	0	0	0	0
DAY 14	MEAN	252.7	--	--	--	--
	S.D.	15.91	--	--	--	--
	N	2	0	0	0	0

-- = Data Unavailable

Table 7.3

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104IP4A

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	5 1-F	10 2-F	16.5 3-F	30 4-F
DAY -2	MEAN	234.6	235.3	239.9	237.3
	S.D.	23.07	22.76	20.45	19.73
	N	5	5	5	5
DAY 0	MEAN	236.8	233.6	239.9	236.0
	S.D.	21.89	22.76	19.59	20.23
	N	5	5	5	5
DAY 7	MEAN	250.4	251.6	259.6	227.0
	S.D.	17.90	25.14	26.54	14.22
	N	5	5	5	3
DAY 14	MEAN	261.0	266.2	269.5	253.4
	S.D.	17.42	29.18	26.77	5.59
	N	5	5	5	2

Table 7.4

**ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS**

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104PO26

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	550 1-F	700 2-F	900 3-F	1150 4-F	1500 5-F
DAY -4	MEAN	198.4	199.4	200.4	202.3	203.2
	S.D.	13.78	11.63	11.04	12.91	12.46
	N	5	5	5	5	5
DAY 0	MEAN	204.3	198.1	199.4	205.1	205.1
	S.D.	18.70	14.51	8.29	15.29	14.11
	N	5	5	5	5	5
DAY 7	MEAN	207.5	200.2	--	208.4	--
	S.D.	0.00	0.00	--	29.77	--
	N	1	1	0	2	0
DAY 14	MEAN	229.5	232.2	--	251.4	--
	S.D.	0.00	0.00	--	44.19	--
	N	1	1	0	2	0

-- = Data Unavailable

Table 7.5.

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104PO6A

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	150	230	350
		1-F	2-F	3-F
DAY -2	MEAN	240.3	239.2	239.2
	S.D.	21.01	20.22	19.71
	N	5	5	5
DAY 7	MEAN	245.8	--	224.2
	S.D.	8.79	--	0.00
	N	3	0	1
DAY 14	MEAN	267.9	--	254.0
	S.D.	17.75	--	0.00
	N	3	0	1

-- = Data Unavailable

Table 7.6

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104P06B

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	40 1-F	80 2-F	150 3-F
DAY -3	MEAN	163.2	164.3	--
	S.D.	11.08	9.24	--
	N	5	5	0
DAY 0	MEAN	165.9	170.0	--
	S.D.	11.31	10.80	--
	N	5	5	0
DAY 7	MEAN	201.1	208.2	--
	S.D.	13.54	14.23	--
	N	5	5	0
DAY 14	MEAN	231.8	241.3	--
	S.D.	14.29	16.48	--
	N	5	5	0

-- = Data Unavailable

Table 7.7

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 104IP26

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	30 1-F	60 2-F	125 3-F	250 4-F	500 5-F
DAY -3	MEAN	199.1	200.1	200.7	197.6	198.0
	S.D.	8.33	11.71	9.26	11.89	10.23
	N	5	5	5	5	5
DAY 0	MEAN	207.5	205.6	204.4	205.2	205.4
	S.D.	10.45	13.98	11.00	11.55	13.33
	N	5	5	5	5	5
DAY 7	MEAN	228.9	232.3	--	--	--
	S.D.	14.62	17.39	--	--	--
	N	5	5	0	0	0
DAY 14	MEAN	253.8	251.4	--	--	--
	S.D.	19.22	19.93	--	--	--
	N	5	5	0	0	0

-- = Data Unavailable

Table 8.1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104P024

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	10 1-F	15 2-F	20 3-F	25 4-F	35 5-F	50 6-F	110 7-F	250 8-F
DAY 7	MEAN	--	--	26.4	--	--	21.6	-4.9	-33.6
	S.D.	--	--	9.01	--	--	7.40	26.70	0.00
	N	0	0	5	0	0	5	4	1
DAY 14	MEAN	--	--	44.9	--	--	15.4	38.9	42.7
	S.D.	--	--	43.95	--	--	26.36	17.16	0.00
	N	0	0	5	0	0	5	3	1
TOTAL GAIN	MEAN	--	--	71.2	--	--	37.0	46.3	9.1
	S.D.	--	--	44.59	--	--	26.19	4.92	0.00
	N	0	0	5	0	0	5	3	1

-- = Data Unavailable

Table 8.1 (Continued)

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104P024

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	600 9-F
DAY 7	MEAN	--
	S.D.	--
	N	0
DAY 14	MEAN	--
	S.D.	--
	N	0
TOTAL GAIN	MEAN	--
	S.D.	--
	N	0

-- = Data Unavailable

Table 8.2

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104IP24

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	20 1-F	50 2-F	110 3-F	250 4-F	600 5-F
DAY 7	MEAN	-5.8	--	--	--	--
	S.D.	4.74	--	--	--	--
	N	2	0	0	0	0
DAY 14	MEAN	35.9	--	--	--	--
	S.D.	13.79	--	--	--	--
	N	2	0	0	0	0
TOTAL GAIN	MEAN	30.1	--	--	--	--
	S.D.	18.53	--	--	--	--
	N	2	0	0	0	0

-- = Data Unavailable

Table 8.3

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104IP4A

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	5 1-F	10 2-F	16.5 3-F	30 4-F
DAY 7	MEAN	13.6	18.0	19.6	-8.0
	S.D.	5.45	5.64	7.90	38.56
	N	5	5	5	3
DAY 14	MEAN	10.6	14.5	9.9	18.6
	S.D.	3.33	5.66	3.65	1.27
	N	5	5	5	2
TOTAL GAIN	MEAN	24.2	32.6	29.6	32.3
	S.D.	4.91	8.86	7.60	13.65
	N	5	5	5	2

Table 8.4

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104PO26

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	550 1-F	700 2-F	900 3-F	1150 4-F	1500 5-F
DAY 7	MEAN	16.8	6.1	--	2.1	--
	S.D.	0.00	0.00	--	2.26	--
	N	1	1	0	2	0
DAY 14	MEAN	22.0	32.0	--	43.0	--
	S.D.	0.00	0.00	--	14.42	--
	N	1	1	0	2	0
TOTAL GAIN	MEAN	38.8	38.1	--	45.1	--
	S.D.	0.00	0.00	--	16.69	--
	N	1	1	0	2	0

-- = Data Unavailable

Table 8.5
ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104PO6A

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	150 1-F	230 2-F	350 3-F
DAY 7	MEAN	21.4	--	1.3
	S.D.	9.45	--	0.00
	N	3	0	1
DAY 14	MEAN	22.1	--	29.8
	S.D.	9.04	--	0.00
	N	3	0	1
TOTAL GAIN	MEAN	43.5	--	31.1
	S.D.	14.78	--	0.00
	N	3	0	1

-- = Data Unavailable

Table 8.6

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104PO6B

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	40 1-F	80 2-F	150 3-F
DAY 7	MEAN	35.2	38.1	--
	S.D.	6.84	4.67	--
	N	5	5	0
DAY 14	MEAN	30.7	33.2	--
	S.D.	1.85	6.89	--
	N	5	5	0
TOTAL GAIN	MEAN	65.9	71.3	--
	S.D.	6.95	10.10	--
	N	5	5	0

-- = Data Unavailable

Table 8.7

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 104IP26

SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	30 1-F	60 2-F	125 3-F	250 4-F	500 5-F
DAY 7	MEAN	21.4	26.7	--	--	--
	S.D.	9.98	9.24	--	--	--
	N	5	5	0	0	0
DAY 14	MEAN	24.9	19.1	--	--	--
	S.D.	6.28	10.20	--	--	--
	N	5	5	0	0	0
TOTAL GAIN	MEAN	46.3	45.8	--	--	--
	S.D.	12.98	6.32	--	--	--
	N	5	5	0	0	0

-- = Data Unavailable

Table 9

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

Dose-Mortality Data

WR242511 Tartrate - Gavage

<u>Dose Level (mg base/kg)</u>	<u>Mortality^a</u>	
	<u>Males</u>	<u>Females</u>
10	0/5	-
15	0/5	-
16.5	3/5	-
18	4/5	-
20	5/5	0/5
25	5/5	-
35	5/5	-
50	5/5	0/5
110	-	2/5
250	-	4/5
600	-	5/5

^anumber of deaths/number of animals in group.

WR242511 Tartrate - Intraperitoneal

<u>Dose Level (mg base/kg)</u>	<u>Mortality^a</u>	
	<u>Males</u>	<u>Females</u>
5	0/5	0/5
10	0/5	0/5
16.5	1/5	0/5
20	4/5	3/5
30	3/5	3/5
50	5/5	5/5
110	5/5	5/5
250	4/5	5/5
600	5/5	5/5

^anumber of deaths/number of animals in group.

Table 9 (contd.)

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS
Dose-Mortality Data

WR269410 - Gavage

<u>Dose Level (mg/kg)</u>	<u>Mortality^a</u>	
	<u>Males</u>	<u>Females</u>
40	0/5	0/5
80	0/5	2/5
150	0/5	2/5
230	2/5	5/5
350	4/5	4/5
550	2/5	4/5
700	2/5	4/5
900	4/5	5/5
1150	3/5	3/5
1500	5/5	5/5

^anumber of deaths/number of animals in group.

WR269410 -Intraperitoneal

<u>Dose Level (mg base/kg)^b</u>	<u>Mortality^a</u>	
	<u>Males</u>	<u>Females</u>
35 (30)	0/5	0/5
43 (50)	0/5	0/5
134 (125)	3/5	5/5
215 (250)	3/5	5/5
473 (500)	4/5	5/5

^anumber of deaths/number of animals in group

^bactual (intended) dose level

DRAFT

APPENDIX 1

Analytical Chemistry Methodology and Dosage Formulation Analysis

DRAFT

INITIAL PURITY AND IDENTITY STUDY AND SAMPLES IN 1% METHYLCELLULOSE AND 0.4% TWEEN 80 ANALYSIS OF 8-[(4-AMINO-1-METHYLBUTYL)AMINO]-5-(1-HEXYLOXY-6-METHOXY-4-METHYLQUINOLINE DL-TARTRATE (WR242511). STUDY NO. 104

ANALYSTS: ADAM NEGRUSZ
A.KARL LARSEN, JR.

STUDY SITE: FORENSIC TOXICOLOGY LABORATORY
COLLEGE OF PHARMACY
UNIVERSITY OF ILLINOIS AT CHICAGO
CHICAGO, ILLINOIS 60612

SPONSOR: TOXICOLOGY RESEARCH LABORATORY
UNIVERSITY OF ILLINOIS AT CHICAGO
CHICAGO, ILLINOIS 60612

REPORT PREPARED: JULY 12, 1993

APPROVED: JULY 12, 1993
DR. EUGENE F. WOODS, Ph.D.



DRAFT

OBJECTIVE

The objective of this study was to confirm the initial identity, establish the purity of WR242511 and to develop the analytical method for dosage formulation analysis.

WR242511 samples were submitted for analysis May 26, 1993 and June 3, 1993. Results are found on pages 9 and 10.

In low concentration WR242511 is stable for 48 hours (<10% loss). In high concentration drug is stable during two weeks period of time. This will be reported with the longer term toxicological studies.

EXPERIMENTAL

The subject sample - WR242511 was supplied by the Toxicology Research Laboratory and stored at -20°C when it was not analyzed.

Description

A fine yellow powder, no obvious odor.

Spectrum

An ultraviolet spectrum (Figure I) recorded on a Shimadzu Spectronic 200 UV spectrometer (dual beam), was obtained from 20 ug/ml solution of WR242511 prepared in mobile phase. The sample was found with maximal absorptivity observed at 212 nm and 264 nm.

ANALYTICAL METHOD

Reagents

Subject sample (WR242511) was supplied by Toxicology Research Laboratory. HPLC grade methanol, acetonitrile, ammonium formate and formic acid were purchased from Fisher Scientific. HPLC grade water was supplied through a Millipore, MILLI-Q Reagent Water System which was fed with distilled water.

Standards

All WR242511 concentrations reflect free base value. A 0.71 mg base/ml WR242511 stock solution was prepared by weighing 100 mg of DL-tartrate salt (mole fraction = 0.71) into 100 ml volumetric flask. The content was dissolved in and the volume brought to mark with mobile phase. Calibration standard solutions were prepared in mobile phase using 0.71 mg base/ml WR242511 stock solution as follows.

<u>Volume Transferred (ml)</u>	<u>Flask Volume (ml)</u>	<u>Final Concentration (ug base/ml)</u>
1.0	100	7.1
2.0	100	14.2
4.0	100	28.4
6.0	100	42.6
8.0	100	56.8
10.0	100	71.0

Aliquots of 0.5 ml from each calibration standard solution were transferred to individually labelled crimp-top vials, sealed and stored at -20°C until analyzed.

Controls

Control A (0.639 mg base/ml), control B (2.84 mg base/ml) and control C (7.81 mg base/ml) were prepared by weighing 90 mg, 400 mg and 1100 mg respectively of WR242511 DL-tartrate salt into three 100 ml volumetric flasks, dissolved in and diluted to mark with mobile phase. Aliquots of 1.5 ml of each control were transferred to individually labelled screw-capped vials, sealed and stored at -20°C until analyzed.

Analytical Procedure

One set of WR242511 calibration standards and three vials of each stock control solutions were removed from a -20°C freezer to warm up prior to samples analysis. Working control solutions were prepared as follows. Control A - 1 ml of stock solution was transferred to a 25 ml volumetric flask and diluted to mark with mobile phase. Control B - 1 ml of stock solution was transferred to a 25 ml volumetric flask and diluted to mark with mobile phase. Five ml were then transferred to another 25 ml volumetric flask and diluted to mark with mobile phase. Control C was prepared the same way as control B. The standard curve was run at the beginning and at the end of the day. Controls were analyzed in a random order.

HPLC System

See PURITY section, WR242511 was monitored at 230 nm.

Calculations

A standard curve was run at the beginning and the end of the day. Final concentration for controls and samples were determined using a composite standard curve. The composite standard curve was determined by linear least squared regression analysis of the peak areas for WR242511 as a function of concentration. WR242511 concentrations (mg base/ml) for controls and samples were determined using the following equation:

$$\text{WR242511 conc.} = (Y-B)/M \times (\text{d.f.}/1000)$$

Y - peak area

B - Y-intercept from regression analysis of composite standard curve

M - slope from regression analysis

d.f. - dilution factor

PURITY

HPLC System

Solvent Delivery System:	Perkin-Elmer Series 3B Pump
Injector:	Rheodyne 7125 with 50 ul sample loop
Analytical Column:	Spherisorb CN 5u, 250 mm x 4.6 mm (Alltech)
Detector:	Perkin-Elmer LC-55B UV Detector, 225 nm, 264 nm
Integrator:	Spectra-Physics SP4270 Integrator

Mobile Phase: 20% methanol, 50% acetonitrile, 30% 0.01 M ammonium formate (in water), Ph 3.0 (adjusted with 88% formic acid), flow 1.5 ml/minute

Procedure

Six solutions of WR242511 were prepared as follows. Twenty five mg of WR242511 sample was weighed into a 25 ml volumetric flask. The sample was dissolved in and the volume brought to mark with mobile phase. A 50 ul aliquot of each solution was immediately chromatographed at 225 nm and next at 264 nm.

Calculation of Results

Quantitations were based on the assumption of equal detector response per unit weight of all UV-absorbing components. Areas of WR242511 and other detectable components in the subject sample chromatograms were employed in the following equation to calculate the percentage of WR242511 present in the sample:

$$\% \text{PURITY} = (\text{area of WR242511} / \text{total area}) \times 100$$

Results

Typical chromatogram is shown in Figure II. The subject sample was found to contain less than 1% of one UV-absorbing impurity (225 nm). At 264 nm no visible impurities were observed. Percent purity of WR242511 was found to be 99.51%, standard deviation - 0.02%. The assay results are presented in Table I.

IDENTIFICATION

GC-MS System

Gas Chromatograph:	Hewlett-Packard Series II
Mass Selective Detector:	Hewlett-Packard Model 5970
Analytical Column:	30 m x 0.25 mm ID, DB-5 with a 3 micron film thickness.
GC Parameters:	injector temp. 250°C, oven temp. 70°C initial, 280°C final, 15°C/minute ramp, carrier gas - helium, flow rate 2 ml/minute, split ratio 10:1

Procedure

Subject sample (WR242511) was submitted from the Toxicology Research Laboratory. The sample was dissolved in methanol to a concentration of 0.71 ug base/ml and a 2 ul aliquot was injected on the column. The MSD scanned from 40 amu to 400 amu at rate of 1 scan per second.

Results - GC-MS

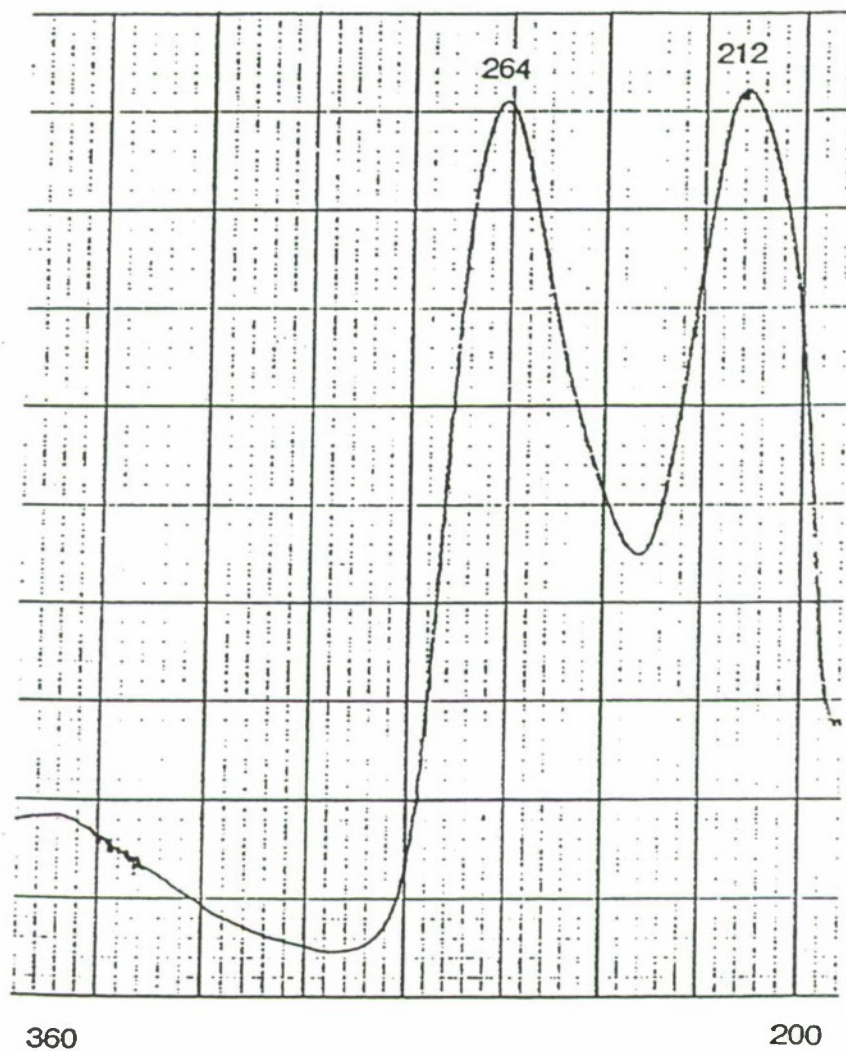
The mass spectrum indicates a molecular ion m/e 373 which is in agreement with the WR242511 molecular weight. Major fragments of WR242511 sample are m/e 84, 175, 203, 288.

Figure III shows the mass spectrum of the initial WR242511 sample.

DRAFT

FIGURE I

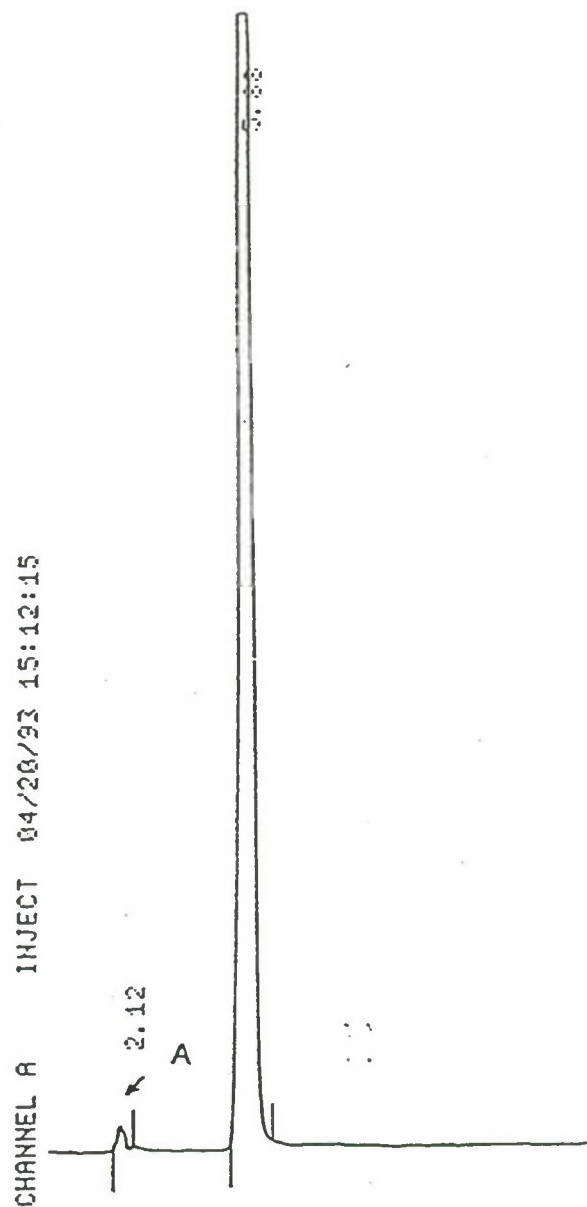
ULTRAVIOLET SPECTRUM OF WR242511



DRAFT

FIGURE II

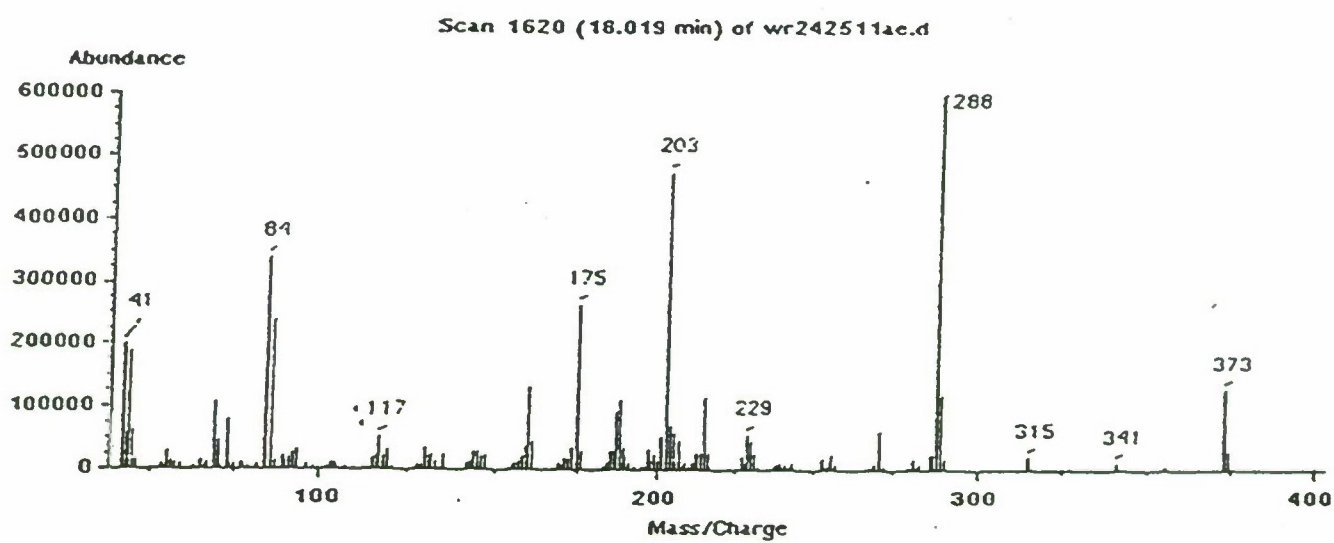
CHROMATOGRAM OF WR242511 SAMPLE (CONCENTRATION 0.71 MG BASE/ML, 225 NM)



DRAFT

FIGURE III

MASS SPECTRUM OF INITIAL WR242511 SAMPLE



DRAFT

TABLE I

PURITY DATA FOR WR242511 PRIOR TO INITIATING STUDY NO. 104

Solutions

Peak Identity	1	2	3	4	5	6
A	4370	4354	4307	4414	3925	4509
WR242511	871097	863423	869317	869227	872867	862653
% Purity	99.501	99.498	99.507	99.495	99.552	99.480

Mean \pm S.D. - 99.505 \pm 0.024

DRAFT

MEMO

DATE: May 26, 1993
TO: Dr. Barry S. Levine
FROM: Adam Negrusz
Forensic Toxicology Laboratory
College of Pharmacy
RE: WR242511 samples submitted for analysis May 26, 1993.

WR242511 Concentration
(mg base/ml)

Sample Identification	Mean (\pm SD)
LIGHT GREEN WITH BLUE DOT (2.0)	1.9010 (\pm 0.0078)
GREEN (3.0)	2.7401 (\pm 0.0023)
YELLOW (4.0)	3.9661 (\pm 0.0077)
PINK (5.0)	4.5820 (\pm 0.0124)
PINK WITH BLUE DOT (7.0)	6.4099 (\pm 0.0109)
GREEN WITH BLUE DOT (10.0)	9.7111 (\pm 0.0889)
BROWN (22.0)	21.5021 (\pm 0.1055)
BLACK WITH WHITE DOT (50.0)	49.5947 (\pm 0.1897)
BLACK WITH YELLOW DOT (120.0)	123.6744 (\pm 0.4024)

DRAFT

MEMO

DATE: June 3, 1993
TO: Dr. Barry S. Levine
FROM: Adam Negrusz
Forensic Toxicology Laboratory
College of Pharmacy
RE: WR242511 samples submitted for analysis June 3, 1993.

WR242511 Concentration
(mg base/ml)

Sample
Identification

Mean (\pm SD)

PINK WITH WHITE DOT (6.0)	6.3654 (\pm 0.0770)
GREEN WITH BLACK DOT (3.6)	3.6226 (\pm 0.0329)
BLUE WITH BLACK DOT (3.3)	3.2903 (\pm 0.0241)
LIGHT GREEN (2.0)	1.9403 (\pm 0.0139)
LEMON YELLOW (1.0)	1.0041 (\pm 0.0039)

DRAFT

INITIAL PURITY, IDENTITY AND SAMPLES ANALYSIS IN 1%
METHYLCELLULOSE AND 0.4% AND 0.2% TWEEN 80 OF
p-AMINOHEPTANOPHENONE (WR269410). STUDY NO. 104

ANALYSTS:

ADAM NEGRUSZ
A. KARL LARSEN, JR.

STUDY SITE:

FORENSIC TOXICOLOGY LABORATORY
COLLEGE OF PHARMACY
UNIVERSITY OF ILLINOIS AT CHICAGO
CHICAGO, ILLINOIS 60612

SPONSOR:

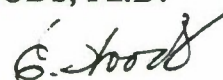
TOXICOLOGY RESEARCH LABORATORY
UNIVERSITY OF ILLINOIS AT CHICAGO
CHICAGO, ILLINOIS 60612

REPORT PREPARED:

JULY 12, 1993

APPROVED:

JULY 12, 1993
DR. EUGENE F. WOODS, Ph.D.



OBJECTIVE

The objective of this study was to confirm the initial identity and establish the purity of WR269410 and to develop the analytical method for dosage formulation analysis.

WR269410 samples were submitted for analysis May 25, 27, 1993 and June 3, 22, 1993. Results are found on pages 9, 10 and 11.

In low and in high concentrations WR269410 is stable for two weeks (<10% loss). This will be reported with the longer term toxicological studies.

EXPERIMENTAL

The subject sample - WR269410 was supplied by the Toxicology Research Laboratory and stored at -20°C when it was not analyzed.

Description

A fine white powder, no obvious odor.

Spectrum

An ultraviolet spectrum (Figure I) recorded on a Shimadzu Spectronic 200 UV spectrometer (dual beam) was obtained from 20 ug/ml solution of WR269410 prepared in mobile phase. The sample was found with maximal absorptivity observed at 230 nm and 312 nm.

ANALYTICAL METHOD

Reagents

Subject sample (WR269410) was supplied by the Toxicology Research Laboratory. HPLC grade methanol, acetonitrile and acetic acid glacial were purchased from Fisher Scientific, 1-heptanosulfonate sodium salt from Regis. HPLC grade water was supplied through a Millipore, MILLI-Q Reagent Water System which was fed with distilled water.

Standards

A 1.0 mg/ml of WR269410 stock solution was prepared by weighing 100 mg of WR269410 into 100 ml volumetric flask. The content was dissolved in and the volume brought to mark with mobile phase. Calibration standards solutions were prepared in mobile phase using 1.0 mg/ml WR269410 stock solution as follows.

Volume Transferred (ml)	Flask Volume (ml)	Final Concentration ($\mu\text{g/ml}$)
1.0	100	10.0
2.0	100	20.0
4.0	100	40.0
6.0	100	60.0
8.0	100	80.0
10.0	100	100.0

Aliquots of 0.5 ml from each calibration standard solution were transferred to individually labelled crimp-top vials, sealed and stored at -20°C until analyzed.

Controls

Control A (9 mg/ml), control B (50 mg/ml), and control C (110 mg/ml) were prepared by weighing 900 mg, 5000 mg and 11000 mg respectively of WR269410 into three 100 ml volumetric flasks, dissolved in and diluted to mark with mobile phase. Aliquots of 1.5 ml of each control were transferred to individually labelled screw-capped vials, sealed and stored at -20°C until analyzed.

Analytical Procedure

One set of WR269410 calibration standards and three vials of each stock control solutions were removed from a -20°C freezer to warm up prior to samples analysis. Working control solutions were prepared as follows. Control A - 1 ml of stock solution was transferred to a 25 ml volumetric flask and diluted to mark with mobile phase, 5 ml then were then transferred to a 25 ml volumetric flask and diluted to mark with mobile phase. Control B - 1 ml of stock was transferred to a 25 ml volumetric flask and diluted to mark with mobile phase. One milliliter was then transferred to another 25 ml volumetric flask and diluted to mark with mobile phase. Control C - 1 ml of stock solution was transferred to 100 ml volumetric flask and diluted to mark with mobile phase. One milliliter was then transferred to a 25 ml volumetric flask and diluted to mark with mobile phase. The standard curve was run at the beginning and at the end of the day. Controls were analyzed in a random order.

HPLC System

See PURITY section, WR269410 was monitored at 254 nm.

DRAFT

PURITY

HPLC System

Solvent Delivery System: Perkin-Elmer Series 3B Pump

Injector: Rheodyne 7125 with 20 ul sample loop

Analytical Column: uBondapak C18, 300 mm x 3.9 mm (Waters)

Detector: Kratos Spectroflow 773 UV Detector, 0.010 AUFS, 230nm and 312nm

Integrator: 3380A Hewlett-Packard Integrator

Mobile Phase: 60% of acetonitrile and 40% of 0.01 M heptanosulfonate sodium salt in 0.1% (v/v) acetic acid (in water), flow 1.5 ml/minute

Procedure

Six solutions of WR269410 were prepared as follows. Twenty five mg of WR269410 sample was weighed into a 25 ml volumetric flask. The sample was dissolved in and the volume brought to mark with mobile phase. A 20 ul aliquot of each solution was immediately chromatographed at 230 nm and next at 312 nm.

Results

Typical chromatograms are shown in Figure II. The initial purity study of WR269410 shows that there are no UV absorbing impurities (230 nm, 312 nm) and from this point of view the substance is 100% pure.

IDENTIFICATION

GC-MS System

Gas Chromatograph: Hewlett-Packard Series II

Mass Selective Detector: Hewlett-Packard Model 5970

Analytical Column: 30 m x 0.25 mm ID, DB-1 with a 3 micron film thickness.

DRAFT

GC Parameters:

injector temp. 250°C, oven temp. 70°C initial, 280°C final,
20°C/minute ramp, carrier gas - helium, flow rate 2 ml/minute,
split ratio 10:1

Procedure

Subject sample (WR269410) was submitted from the Toxicology Research Laboratory. The sample was dissolved in methanol to a concentration of 1 ug/ml and a 2 ul aliquot was injected on the column. The MSD scanned from 40 amu to 400 amu at a rate of 1 scan per second.

Results - GS-MS

The mass spectrum indicates a molecular ion m/e 205 which is in agreement with the WR269410 molecular weight. Major fragments of the sample are m/e 41, 65, 92, 120, 135, 148.

Figure III shows the mass spectrum of the initial WR269410 sample.

DRAFT

FIGURE I

ULTRAVIOLET SPECTRUM OF WR269410

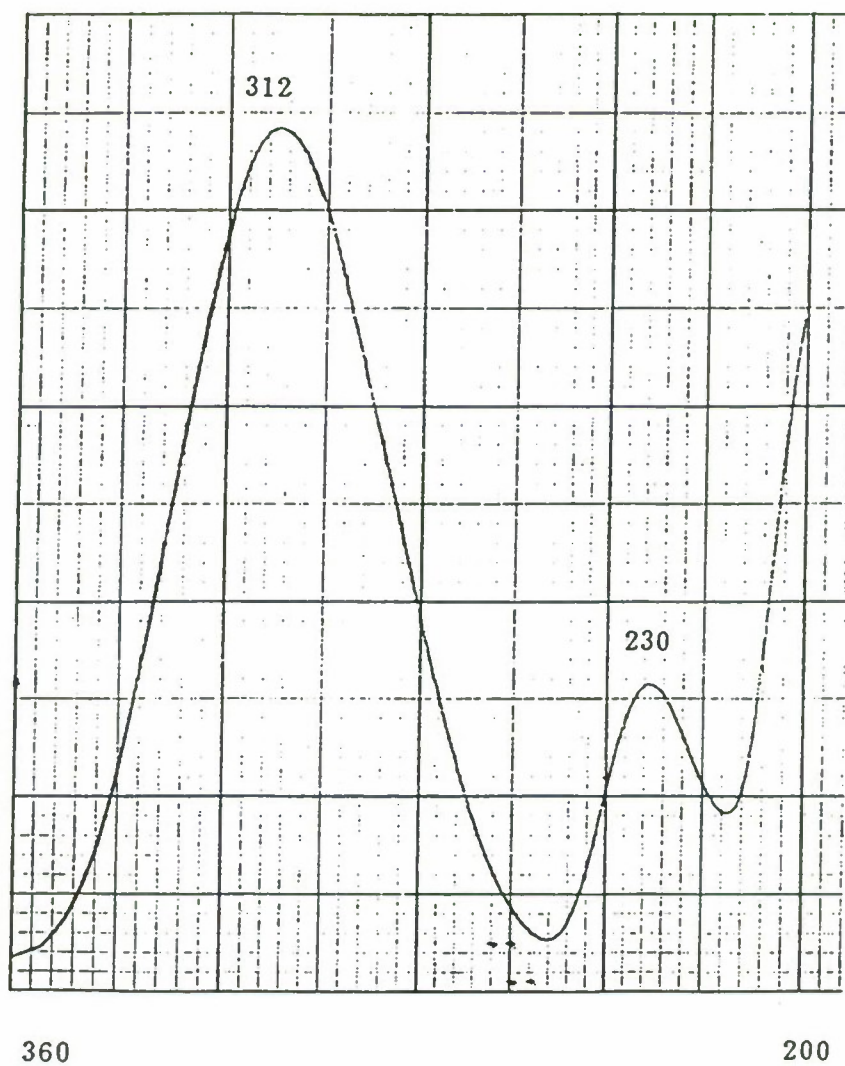
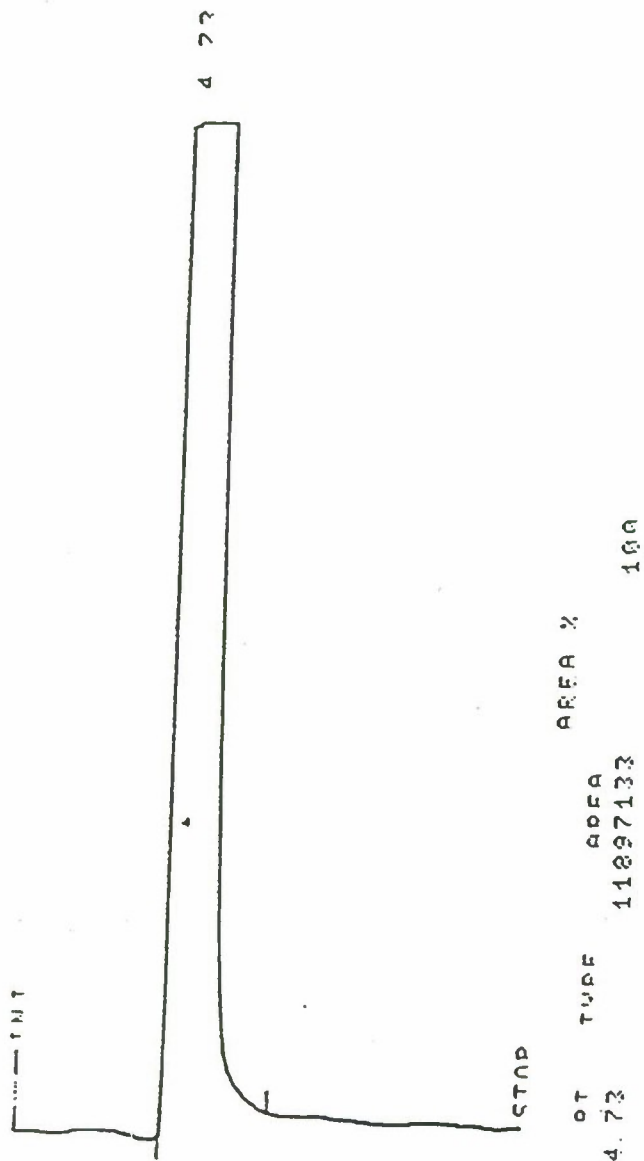


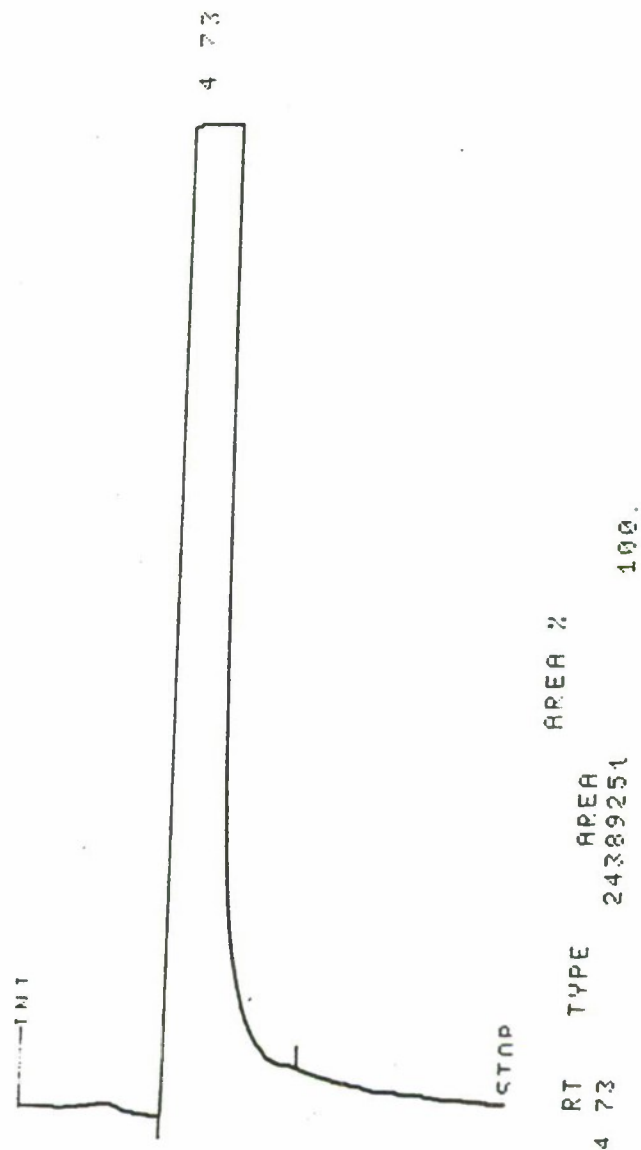
FIGURE II

DRAFT

CHROMATOGRAMS OF WR269410 AT 230 NM
(A) AND 312 NM (B), CONCENTRATION 1 MG/ML



A

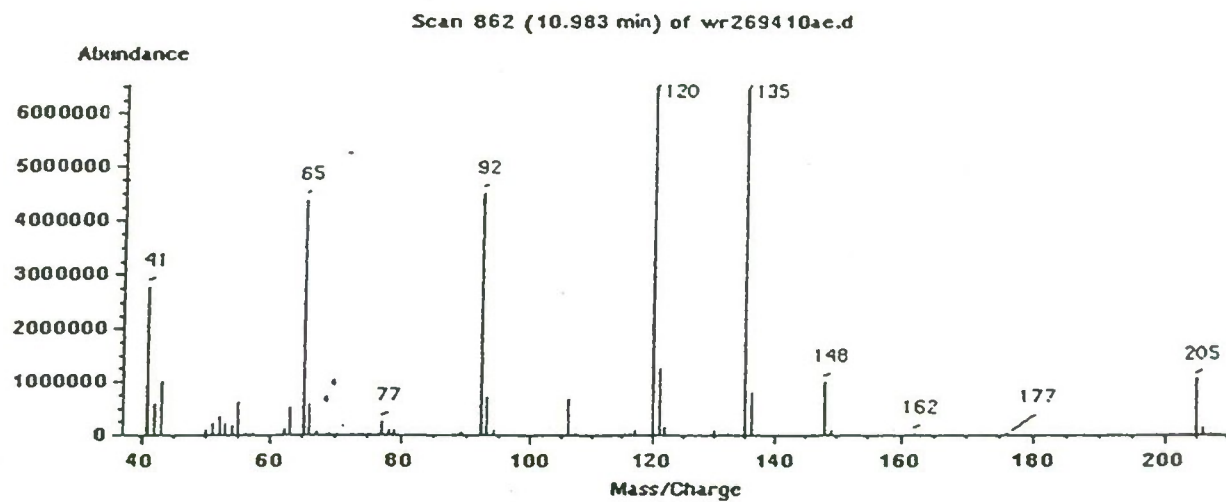


B

DRAFT

FIGURE III

MASS SPECTRUM OF INITIAL WR269410 SAMPLE



DRAFT

MEMO

DATE: May 27, 1993
TO: Dr. Barry S. Levine
FROM: Adam Negrusz
Forensic Toxicology Laboratory
College of Pharmacy
RE: WR269410 samples submitted for analysis May 25, 1993 and May 27, 1993.

WR269410 Concentration
(mg/ml)

Sample Identification	Mean (\pm SD)
LIGHT ORANGE (27.5)	26.6967 (\pm 0.2284)
LIGHT GREEN, DARK ORANGE (35.0)	34.9143 (\pm 0.2858)
DARK ORANGE, BROWN (45.0)	47.3398 (\pm 0.1992)
GREEN, BROWN (57.5)	61.5332 (\pm 0.1389)
YELLOW, BLACK (75.0)	71.4507 (\pm 0.2701)

MEMO

DRAFT

DATE: June 3, 1993
TO: Dr. Barry S. Levine
FROM: Adam Negrusz
Forensic Toxicology Laboratory
College of Pharmacy
RE: WR269410 samples submitted for analysis June 3, 1993.

WR269410 Concentration
(mg/ml)

Sample
Identification

Mean (\pm SD)

DARK GREEN, BLUE (7.5)	8.0820 (\pm 0.1122)
LIGHT ORANGE WITH YELLOW DOT (11.5)	11.4596 (\pm 0.0310)
BROWN WITH BLACK DOT (17.5)	19.0269 (\pm 0.1575)

MEMO

DRAFT

DATE: June 22, 1993
TO: Dr. Barry S. Levine
FROM: Adam Negrusz
Forensic Toxicology Laboratory
College of Pharmacy
RE: WR269410 samples submitted for analysis June 22, 1993.

WR269410 Concentration
(mg/ml)

Sample Identification	Mean (\pm SD)
BROWN, BLACK (2.0)	2.1323 (\pm 0.0034)
LIGHT ORANGE, BLUE (4.0)	4.3007 (\pm 0.0601)
GREEN, BLUE (7.5)	7.8245 (\pm 0.0264)

DRAFT

APPENDIX 2

Analytical Chemistry Report
from Dr. Flanagan (Univ. of Iowa)

DRAFT

**Analysis of p-Aminoheptanophenone (WR269410) Solutions in PEG 200
After Toxicological Testing**

Douglas R. Flanagan, Ph.D.
Siriporn Toongsuwan, B.S.
Kirk VanDer Kamp, B.S.

July 21, 1993

Contract No. DAMD 17-92-C-2035

College of Pharmacy
University of Iowa
Iowa City, IA 52242
(319) 335-8824

DRAFT

Analysis of p-Aminoheptanophenone (WR269410) Solution in PEG 200 After Toxicological Testing

Summary

PEG 200 solutions of WR269410 were analyzed for content after receipt from the University of Illinois (Dr. Barry Levine).

Assay Procedure

1. Make fresh standard solution (about 10 µg/mL) of PAHP in 95% ethanol.
2. Dilute PAHP in PEG 200 solutions that were send from UIC with 95% ethanol (dilution factor = 10,000) by diluting 1 mL of the sample to 100 mL and then diluting 1 mL of this solution to 100 mL with 95% ethanol.
3. Assay the concentration of the solutions by using the HP 8450 UV spectrophotometer.
4. Concentration of the samples were calculated as follow:

$$\text{sample conc.} = (\text{std conc.} * \text{Abs}_{\text{sample}}) * 10,000 / \text{Abs}_{\text{std}}$$

Assay Results

The results from the UV assay of PAHP solutions are shown in Tables 1, 2 and 3.

Table 1: UV Assay Data of PAHP Solutions Returned from UIC on
05/21/93; Mouse Study

Labeled Conc. (mg/mL)	Experimental Conc. (mg/mL)
20	18.2
24	26.4
28	31.3
34	31.7
40	40.3
55	50.3
65	66.8
75	77.6
87.5	84.2

DRAFT

TABLE 2: UV Assay Data of PAHP Solutions Returned from UIC on
07/08/93; Rat Study

Labeled Conc. (mg/mL)	Experimental Conc. (mg/mL)
6	6.9
12	8.5
25	26.7
50	42.9
100	94.5

TABLE 3: UV Assay Data of PAHP Solutions Returned from UIC on
07/08/93; Mouse Study

Labeled Conc. (mg/mL)	Experimental Conc. (mg/mL)
80	73.2

DRAFT

APPENDIX 3
Individual Clinical Signs

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 1-M
DOSE: 10 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
491	Hunched Posture			DAY 3	DAY 4	2
	Normal			DAY 8	DAY 9	2
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
492	Normal			DAY 8	DAY 8	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
493	Normal			DAY 8	DAY 13	6
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 7	7
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
494	Normal			DAY 8	DAY 11	4
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	9
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
495	Normal			DAY 11	DAY 11	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 2-M
DOSE: 15 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
496	Normal			DAY 12	DAY 12	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
497	Hunched Posture			DAY 5	DAY 5	1
	Normal			DAY 8	DAY 9	2
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
498	Hunched Posture			DAY 5	DAY 5	1
	Normal			DAY 8	DAY 8	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
499	Hunched Posture			DAY 4	DAY 6	3
	Normal			DAY 8	DAY 8	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
500	Hunched Posture			DAY 5	DAY 7	3
	Normal			DAY 9	DAY 12	3
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	10
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 3-M
DOSE: 20 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
501	Decreased Activity	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
502	Animal Found Dead			DAY 2	DAY 2	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
503	Animal Found Dead			DAY 2	DAY 2	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
504	Decreased Activity	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
505	Decreased Activity	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

<u>Severity No.</u>	<u>Description</u>
1	Slight
2	Moderate
3	Severe

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 4-M
DOSE: 25 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
511	Animal Found Dead			DAY 3	DAY 3	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
512	Animal Found Dead			DAY 3	DAY 3	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
513	Animal Found Dead			DAY 3	DAY 3	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
514	Decreased Activity	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 3	DAY 3	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
515	Decreased Activity	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 3	DAY 3	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 5-M
DOSE: 35(mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
516	Decreased Activity	3		DAY 2	DAY 2	1
	Dark Material Around Nose			DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Labored Breathing			DAY 2	DAY 2	1
	Lethargic			DAY 2	DAY 2	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
517	Decreased Activity	2		DAY 2	DAY 2	1
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
518	Decreased Activity	2		DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
519	Decreased Activity	2		DAY 2	DAY 3	2
	Animal Found Dead			DAY 4	DAY 4	1
	Hunched Posture			DAY 2	DAY 3	2
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 3	3
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
520	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 6-M
DOSE: 50 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
521	Ataxia	1		DAY 3	DAY 3	1
	Decreased Activity	1		DAY 3	DAY 3	1
	Animal Found Dead			DAY 4	DAY 4	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 3	3
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
522	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 3			DAY 0	DAY 0	1
523	Decreased Activity	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 2	2
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
524	Decreased Activity	1		DAY 1	DAY 2	2
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
525	Decreased Activity	1		DAY 1	DAY 2	2
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 2	2

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 6-M
DOSE: 50 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO4A
DAY 0-DAY 14

GROUP: 1-M
DOSE: 16.5 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
486	Activity Decreased	1		DAY 3	DAY 3	1
	Animal Found Dead			DAY 4	DAY 4	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 3	3
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
487	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 2	DAY 2	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
488	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 2	DAY 2	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
489	Hunched Posture			DAY 1	DAY 12	7
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
490	Hunched Posture			DAY 1	DAY 13	8

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO4A
DAY 0-DAY 14

GROUP: 1-M
DOSE: 16.5 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 6	2
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO4A
DAY 0-DAY 14

GROUP: 2-M
DOSE: 18.0 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
481	Activity Decreased	1		DAY 10	DAY 13	3
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 3	DAY 3	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
482	Activity Decreased	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
483	Activity Decreased	1		DAY 1	DAY 2	2
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
484	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO4A
DAY 0-DAY 14

GROUP: 2-M
DOSE: 18.0 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
485	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 1-M
DOSE: 20 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
551	Decreased Activity	1		DAY 1	DAY 1	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Dark Material Around Nose			DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Labored Breathing			DAY 2	DAY 2	1
	Lethargic			DAY 2	DAY 2	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
552	Decreased Activity	1		DAY 1	DAY 1	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
553	Decreased Activity	1		DAY 2	DAY 3	2
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Dark Material Around Eyes			DAY 3	DAY 3	1
	Dark Material Around Nose			DAY 2	DAY 3	2
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 3	3
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 1-M
DOSE: 20 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
554	Abdomen Bloated			DAY 2	DAY 13	9
	Decreased Activity	1		DAY 4	DAY 4	1
	Decreased Activity	2		DAY 3	DAY 7	2
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Dark Material Around Eyes			DAY 3	DAY 3	1
	Dark Material Around Nose			DAY 2	DAY 3	2
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
555	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 2-M
DOSE: 50 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
561	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
562	Blue Feet 2			DAY D	DAY D	1
	Decreased Activity	1		DAY 1	DAY 1	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY D	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY D	1
563	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY D	DAY D	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY D	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY D	DAY D	1
564	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY D	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 2-M
DOSE: 50 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
565	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 3-M
DOSE: 110 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
571	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	3		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
572	Third Clinical Sign			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
573	Second Clinical Sign			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
574	Third Clinical Sign			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
575	Second Clinical Sign			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 3-M
DOSE: 110 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1

Severity Codes

<u>Severity No.</u>	<u>Description</u>
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 4-M
DOSE: 250 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
581	Abdomen Bloated			DAY 2	DAY 13	7
	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 7	3
	Decreased Activity	2		DAY 2	DAY 4	3
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	2		DAY 0	DAY 0	1
	Dark Material Around Nose			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Abdominal Lesion			DAY 9	DAY 13	5
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
582	Second Clinical Sign			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
583	Second Clinical Sign			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
584	Third Clinical Sign			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 4-M
DOSE: 250 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
585	Second Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 5-M
DOSE: 600 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
591	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
592	Third Clinical Sign			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
593	Second Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
594	Second Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
595	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	3		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 1-M
DOSE: 5 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
476	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 6	2
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
477	Hunched Posture			DAY 1	DAY 13	5
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 6	2
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
478	Activity Decreased	1		DAY 10	DAY 11	2
	Hunched Posture			DAY 2	DAY 13	5
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
479	Hunched Posture			DAY 1	DAY 13	5
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 4	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 1-M
DOSE: 5 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
480	Hunched Posture			DAY 1	DAY 12	5
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 4	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 2-M
DOSE: 10(mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
466	Activity Decreased	1		DAY 2	DAY 2	1
	Dark Material Around Nose			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 13	5
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 6	2
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
467	Activity Decreased	1		DAY 9	DAY 9	1
	Hunched Posture			DAY 1	DAY 13	5
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 6	2
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
468	Hunched Posture			DAY 1	DAY 11	4
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 6	3
	Rough Coat			DAY 1	DAY 13	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
469	Activity Decreased	1		DAY 1	DAY 2	2
	Hunched Posture			DAY 1	DAY 11	4
	Hunched Posture 1			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 2-M
DOSE: 10(mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 6	2
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
470	Abdomen Bloated			DAY 2	DAY 2	1
	Activity Decreased	1		DAY 2	DAY 13	2
	Hunched Posture			DAY 1	DAY 11	4
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 4	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 3-M
DOSE: 16.5 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
456	Abdomen Bloated	1		DAY 1	DAY 2	2
	Activity Decreased			DAY 10	DAY 13	4
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 6	2
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
457	Abdomen Bloated	1		DAY 1	DAY 2	2
	Activity Decreased			DAY 10	DAY 13	4
	Dark Material Around Nose			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
458	Abdomen Bloated	1		DAY 1	DAY 9	9
	Activity Decreased			DAY 10	DAY 13	4
	Dark Material Around Nose			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 3-M
DOSE: 16.5 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
459	Abdomen Bloated	1		DAY 1	DAY 9	9
	Activity Decreased			DAY 2	DAY 11	3
	Dark Material Around Nose			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
460	Abdomen Bloated	1		DAY 1	DAY 8	8
	Activity Decreased			DAY 2	DAY 2	1
	Dark Material Around Nose			DAY 1	DAY 1	1
	Animal Found Dead			DAY 9	DAY 9	1
	Hunched Posture			DAY 1	DAY 8	8
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 8	8
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 4-M
DOSE: 30 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
446	Abdomen Bloated			DAY 1	DAY 9	9
	Activity Decreased	1		DAY 1	DAY 13	3
	Activity Decreased	2		DAY 10	DAY 11	2
	Dark Material Around Eyes			DAY 1	DAY 1	1
	Dark Material Around Nose			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
447			DAY 2	DAY 2	1
	Activity Decreased	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
448	Activity Decreased	1		DAY 1	DAY 13	6
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 4-M
DOSE: 30 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
449	Abdomen Bloated			DAY 1	DAY 2	2
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
450	Abdomen Bloated			DAY 1	DAY 3	3
	Activity Decreased	1		DAY 1	DAY 2	2
	Animal Found Dead			DAY 4	DAY 4	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 3	3
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 1-M
DOSE: 550 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
601	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 3	3
	Decreased Activity 1	3		DAY 0	DAY 0	1
	Decreased Activity 3	2		DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Normal			DAY 10	DAY 13	4
	Rough Coat			DAY 1	DAY 9	9
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
602	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 3	3
	Decreased Activity 1	3		DAY 0	DAY 0	1
	Decreased Activity 2	3		DAY 0	DAY 0	1
	Decreased Activity 3	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 6	DAY 13	4
	Rough Coat			DAY 1	DAY 10	9
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
603	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 1-M
DOSE: 550 (mg/kg)

SEX: MALE

ANIMAL # OBSERVATIONS SEVERITY LOC ONSET DURATION FREQUENCY

	Comatose			DAY 1	DAY 1	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Decreased Activity 1	3		DAY 0	DAY 0	1
	Animal Found Dead	.		DAY 2	DAY 2	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
604	Blue Feet			DAY 1	DAY 2	2
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose			DAY 1	DAY 1	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 2	DAY 2	1
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 2	DAY 2	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
605	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 2	DAY 3	2
	Decreased Activity	2		DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 5	3
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 1-M
DOSE: 550 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Normal			DAY 11	DAY 13	3
	Rough Coat			DAY 1	DAY 10	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 2-M
DOSE: 700(mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
611	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 3	DAY 3	1
	Decreased Activity	2		DAY 1	DAY 2	2
	Hunched Posture			DAY 1	DAY 6	5
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Normal			DAY 11	DAY 13	3
	Rough Coat			DAY 1	DAY 10	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
612	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 3	DAY 3	1
	Decreased Activity	2		DAY 1	DAY 2	2
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 6	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 11	DAY 13	3
	Rough Coat			DAY 1	DAY 10	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 2-M
DOSE: 700 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
613	Blue Feet			DAY 1	DAY 2	2
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 1	DAY 2	2
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 2	DAY 2	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
614	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic			DAY 1	DAY 1	1
	Lethargic 2			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
615	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 2-M
DOSE: 700 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 2	DAY 3	2
	Decreased Activity 2	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 4	DAY 5	2
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Normal			DAY 11	DAY 13	3
	Rough Coat			DAY 1	DAY 10	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1
2
3

Slight
Moderate
Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 3-M
DOSE: 900 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
621	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
622	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose			DAY 1	DAY 1	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
623	Ataxia	3		DAY 1	DAY 1	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1
2
3

Slight
Moderate
Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 3-M
DOSE: 900 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Decreased Activity	3		DAY 1	DAY 1	1
	Animal Found Dead			DAY 2	DAY 2	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
624	Ataxia 1			DAY 0	DAY 0	1
	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 2	DAY 3	2
	Decreased Activity	2		DAY 1	DAY 1	1
	Dark Material Around Eyes			DAY 2	DAY 2	1
	Dark Material Around Nose			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 8	8
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
625	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 3-M
DOSE: 900 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 4-M
DOSE: 1150 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
631	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 4	DAY 4	1
	Decreased Activity	2		DAY 2	DAY 3	2
	Decreased Activity	3		DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 6	6
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Normal			DAY 13	DAY 13	1
	Rough Coat			DAY 1	DAY 12	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
632	Ataxia	3		DAY 1	DAY 1	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 4-M
DOSE: 1150 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
633	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
634	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
635	Ataxia 2			DAY 0	DAY 0	1
	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 1	DAY 3	3
	Hunched Posture			DAY 1	DAY 12	10
	Labored Breathing 1			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 4-M
DOSE: 1150 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Lethargic 3			DAY 0	DAY 0	1
	Normal			DAY 13	DAY 13	1
	Rough Coat			DAY 1	DAY 12	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 5-M
DOSE: 1500 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
641	Ataxia	2		DAY 1	DAY 1	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 3	2		DAY 0	DAY 0	1
	Decreased Activity			DAY 1	DAY 1	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
642	Ataxia	3		DAY 1	DAY 1	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Dark Material Around Nose			DAY 1	DAY 1	1
	Animal Found Dead			DAY 2	DAY 2	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1
2
3

Slight
Moderate
Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 5-M
DOSE: 1500 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
643	Ataxia	3		DAY 1	DAY 1	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
644	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
645	Ataxia	3		DAY 1	DAY 1	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 5-M
DOSE: 1500 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 2-M
DOSE: 230 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
431	Ataxia	3		DAY 1	DAY 1	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Blue Tail			DAY 1	DAY 1	1
	Comatose 3			DAY 0	DAY 0	1
	Activity Decreased	3		DAY 1	DAY 1	1
	Activity Decreased 1	2		DAY 0	DAY 0	1
	Activity Decreased 2	2		DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
432	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Blue Tail			DAY 2	DAY 3	2
	Activity Decreased	2		DAY 1	DAY 2	2
	Activity Decreased 1	1		DAY 0	DAY 0	1
	Activity Decreased 2	2		DAY 0	DAY 0	1
	Activity Decreased 3	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 11	6
	Hunched Posture 2			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 8	4
	Rough Coat			DAY 1	DAY 13	9
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
433	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Activity Decreased 1	2		DAY 0	DAY 0	1
	Activity Decreased 2	3		DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 2-M
DOSE: 230 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
434	Activity Decreased 3	2		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Activity Decreased	1		DAY 1	DAY 2	2
	Activity Decreased 1	2		DAY 0	DAY 0	1
	Activity Decreased 2	2		DAY 0	DAY 0	1
	Activity Decreased 3	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 4	DAY 11	3
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 9	5
	Rough Coat			DAY 1	DAY 13	8
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
435	Blue Feet			DAY 1	DAY 4	4
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Activity Decreased	1		DAY 1	DAY 3	3
	Activity Decreased 1	3		DAY 0	DAY 0	1
	Activity Decreased 2	2		DAY 0	DAY 0	1
	Activity Decreased 3	1		DAY 0	DAY 0	1
	Dark Material Around Eyes			DAY 2	DAY 4	3
	Hunched Posture			DAY 1	DAY 13	9
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 2-M
DOSE: 230 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
----------	--------------	----------	-----	-------	----------	-----------

	Normal			DAY 7	DAY 7	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 3-M
DOSE: 350 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
421	Blue Feet			DAY 1	DAY 2	2
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Activity Decreased	1		DAY 2	DAY 11	2
	Activity Decreased	2		DAY 1	DAY 1	1
	Activity Decreased 1	3		DAY 0	DAY 0	1
	Activity Decreased 2	2		DAY 0	DAY 0	1
	Activity Decreased 3	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 13	7
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 7	DAY 8	2
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
422	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Activity Decreased 1	3		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
423	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 3-M
DOSE: 350 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
424	Ataxia	2		DAY 1	DAY 1	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Activity Decreased	3		DAY 1	DAY 1	1
	Activity Decreased 1	3		DAY 0	DAY 0	1
	Activity Decreased 2	3		DAY 0	DAY 0	1
	Activity Decreased 3	3		DAY 0	DAY 0	1
	Dark Material Around Eyes			DAY 1	DAY 1	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
425	Animal Found Dead			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 1-M
DOSE: 40(mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
751	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 12	4
	Rough Coat			DAY 1	DAY 13	9
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
752	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 6	DAY 13	8
	Rough Coat			DAY 1	DAY 5	5
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
753	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 13	5
	Rough Coat			DAY 2	DAY 8	7
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 1-M
DOSE: 40 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
754	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	5
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 6	DAY 13	7
	Rough Coat			DAY 1	DAY 5	5
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
755	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	5
	Rough Coat			DAY 1	DAY 9	8
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 2-M
DOSE: 80(mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
761	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	5
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	2
	Rough Coat			DAY 1	DAY 12	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
762	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 4	DAY 7	3
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 12	2
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
763	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 1	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 2-M
DOSE: 80 (mg/kg)

SEX: MALE

ANIMAL # OBSERVATIONS SEVERITY LOC ONSET DURATION FREQUENCY

	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	4
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	3
	Rough Coat			DAY 1	DAY 11	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
764	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	3
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	2
	Rough Coat			DAY 1	DAY 12	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
765	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 2-M
DOSE: 80 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Hunched Posture			DAY 1	DAY 9	5
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 8	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 3-M
DOSE: 150 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
771	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	2		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 2	DAY 9	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
772	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 2	DAY 9	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
773	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 3-M
DOSE: 150 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
----------	--------------	----------	-----	-------	----------	-----------

	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	2		DAY 0	DAY 0	1
	Decreased Activity	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 2	DAY 9	7
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
774	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 0	DAY 0	1
	Decreased Activity	3		DAY 0	DAY 0	1
	Decreased Activity	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	7
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
775	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Blue Tail			DAY 1	DAY 1	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P06B
DAY 0-DAY 14

GROUP: 3-M
DOSE: 150 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
----------	--------------	----------	-----	-------	----------	-----------

	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 13	8
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 1-M
DOSE: 30 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
651	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity #2	3		DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 3	2
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 13	10
	Rough Coat			DAY 1	DAY 3	3
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
652	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity #1	1		DAY 0	DAY 0	1
	Decreased Activity #2	1		DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 3	2
	Hunched Posture #1			DAY 0	DAY 0	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 13	5
	Rough Coat			DAY 1	DAY 8	8
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
653	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 7	3
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 1-M
DOSE: 30(mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Lethargic #3			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 13	5
	Rough Coat			DAY 1	DAY 8	8
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
654	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 1	DAY 1	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Dark Material Around Nose			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 6	3
	Hunched Posture #1			DAY 0	DAY 0	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 13	4
	Rough Coat			DAY 1	DAY 12	9
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
655	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 6	3
	Hunched Posture #1			DAY 0	DAY 0	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 13	5
	Rough Coat			DAY 1	DAY 8	8

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 1-M
DOSE: 30 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 2-M
DOSE: 60(mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
661	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 1	DAY 1	1
	Decreased Activity #1	3		DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 10	DAY 13	4
	Rough Coat			DAY 1	DAY 9	9
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
662	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity #1	3		DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 11	DAY 13	3
	Rough Coat			DAY 1	DAY 10	10
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
663	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 1	DAY 1	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 2-M
DOSE: 60 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 10	DAY 13	4
	Rough Coat			DAY 1	DAY 9	9
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
664	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 3	DAY 3	1
	Decreased Activity	2		DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Lethargic #3			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 13	4
	Rough Coat			DAY 1	DAY 10	9
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
665	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 3	2
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 2-M
DOSE: 60 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Lethargic #2			DAY 0	DAY 0	1
	Lethargic #3			DAY 0	DAY 0	1
	Normal			DAY 7	DAY 13	5
	Rough Coat			DAY 1	DAY 12	8
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 3-M
DOSE: 125 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
671	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
672	Blue Feet			DAY 1	DAY 1	1
	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Lethargic			DAY 1	DAY 1	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
673	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 2	DAY 3	2
	Decreased Activity	2		DAY 1	DAY 1	1
	Decreased Activity #1	1		DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 3-M
DOSE: 125 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	6
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 13	DAY 13	1
	Rough Coat			DAY 1	DAY 12	12
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
674	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 2	DAY 3	2
	Decreased Activity	3		DAY 1	DAY 1	1
	Decreased Activity #1	2		DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 12	7
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 13	DAY 13	1
	Rough Coat			DAY 1	DAY 12	12
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
675	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 3-M
DOSE: 125 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Labored Breathing #3			DAY 0	DAY 0	1
	Lethargic #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 4-M
DOSE: 250 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
681	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
682	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 3	DAY 3	1
	Decreased Activity #1	3		DAY 0	DAY 0	1
	Decreased Activity #2	3		DAY 0	DAY 0	1
	Decreased Activity #3	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 8	6
	Hunched Posture #1			DAY 0	DAY 0	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Normal			DAY 10	DAY 13	4
	Rough Coat			DAY 1	DAY 9	9
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
683	Blue Feet			DAY 1	DAY 9	2
	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 3	3

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 4-M
DOSE: 250 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Decreased Activity #1	2		DAY 0	DAY 0	1
	Decreased Activity #2	3		DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 8	6
	Hunched Posture #1			DAY 0	DAY 0	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Normal			DAY 13	DAY 13	1
	Rough Coat			DAY 1	DAY 12	12
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
684	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
685	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 5-M
DOSE: 500 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
691	Blue Feet			DAY 1	DAY 1	1
	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 3	DAY 3	1
	Decreased Activity #1	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	9
	Hunched Posture #1			DAY 0	DAY 0	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Lethargic			DAY 1	DAY 1	1
	Lethargic #2			DAY 0	DAY 0	1
	Lethargic #3			DAY 0	DAY 0	1
	Normal			DAY 13	DAY 13	1
	Rough Coat			DAY 1	DAY 12	12
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
692	Blue Feet #1			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
693	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Decreased Activity #1	3		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 5-M
DOSE: 500 (mg/kg)

SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
694	Blue Feet #1			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
695	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 3-F
DOSE: 20(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
506	Normal			DAY 1	DAY 13	8
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Normal 3			DAY 0	DAY 0	1
	Rough Coat			DAY 2	DAY 11	5
	Scheduled Sacrifice			DAY 14	DAY 14	1
507	Normal			DAY 1	DAY 13	9
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Normal 3			DAY 0	DAY 0	1
	Rough Coat			DAY 4	DAY 7	4
	Scheduled Sacrifice			DAY 14	DAY 14	1
508	Normal			DAY 4	DAY 13	7
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 7	6
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
509	Normal			DAY 6	DAY 13	7
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 7	6
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
510	Normal			DAY 1	DAY 13	8
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Normal 3			DAY 0	DAY 0	1
	Rough Coat			DAY 3	DAY 8	5
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 6-F
DOSE: 50 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
526	Normal			DAY 8	DAY 13	5
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 12	8
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
527	Hunched Posture			DAY 1	DAY 7	5
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	4
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 12	9
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
528	Hunched Posture			DAY 0	DAY 1	2
	Normal			DAY 8	DAY 13	4
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 12	9
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
529	Hunched Posture			DAY 5	DAY 7	3
	Normal			DAY 8	DAY 13	2
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 12	11
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
530	Hunched Posture			DAY 1	DAY 6	3
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	5
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 12	8
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 7-F
DOSE: 110 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
531	Decreased Activity	1		DAY 4	DAY 4	1
	Hunched Posture			DAY 2	DAY 7	4
	Normal			DAY 13	DAY 13	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 12	12
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
532	Decreased Activity	1		DAY 4	DAY 4	1
	Hunched Posture			DAY 3	DAY 7	5
	Normal			DAY 11	DAY 13	2
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Normal 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 12	11
	Scheduled Sacrifice			DAY 14	DAY 14	1
533	Decreased Activity	1		DAY 4	DAY 7	2
	Animal Found Dead			DAY 8	DAY 8	1
	Hunched Posture			DAY 2	DAY 7	5
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 7	7
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
534	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Normal 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 3			DAY 0	DAY 0	1
535	Decreased Activity	1		DAY 4	DAY 4	1
	Hunched Posture			DAY 1	DAY 7	6
	Normal			DAY 12	DAY 13	2

Severity Codes

Severity No.

Description

1
2
3

Slight
Moderate
Severe

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 7-F
DOSE: 110 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 11	11
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 8-F
DOSE: 250 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
536	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
537	Decreased Activity	1		DAY 4	DAY 10	4
	Decreased Activity	2		DAY 6	DAY 6	1
	Dark Material Around Eyes			DAY 11	DAY 12	2
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
538	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 0	DAY 2	3
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
539	Ataxia	1		DAY 4	DAY 4	1
	Animal Found Dead			DAY 5	DAY 5	1
	Hunched Posture			DAY 1	DAY 4	4
	Hunched Posture 3			DAY 0	DAY 0	1
	Labored Breathing			DAY 2	DAY 2	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 4	4
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 8-F
DOSE: 250 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
540	Decreased Activity	1		DAY 1	DAY 2	2
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Dark Material Around Eyes			DAY 2	DAY 2	1
	Dark Material Around Nose			DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 9-F
DOSE: 600 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
541	Decreased Activity 2	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
542	Decreased Activity	1		DAY 1	DAY 1	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
543	Decreased Activity	2		DAY 1	DAY 1	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
544	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
545	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture2			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104P024
DAY 0-DAY 14

GROUP: 9-F
DOSE: 600 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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Hunched Posture 3

DAY 0 DAY 0 1

Normal 1

DAY 0 DAY 0 1

Rough Coat 2

DAY 0 DAY 0 1

Rough Coat 3

DAY 0 DAY 0 1

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 1-F
DOSE: 20(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
556	Abdomen Bloated			DAY 2	DAY 2	1
	Dark Material Around Nose			DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
557	Abdomen Bloated			DAY 2	DAY 2	1
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
558	Abdomen Bloated			DAY 2	DAY 13	11
	Dark Material Around Nose			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Lethargic			DAY 7	DAY 7	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
559	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 1-F
DOSE: 20 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
560	Abdomen Bloated			DAY 2	DAY 13	12
	Hunched Posture			DAY 1	DAY 13	11
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 2-F
DOSE: 50 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
566	Abdomen Bloated			DAY 2	DAY 2	1
	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Dark Material Around Nose			DAY 2	DAY 2	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
567	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
568	Abdomen Bloated			DAY 2	DAY 2	1
	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Dark Material Around Nose			DAY 2	DAY 2	1
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 2-F
DOSE: 50(mg/kg)

SEX: FEMALE

ANIMAL # OBSERVATIONS SEVERITY LOC ONSET DURATION FREQUENCY

	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
569	Abdomen Bloated			DAY 2	DAY 2	1
	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Lethargic			DAY 2	DAY 2	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
570	Abdomen Bloated			DAY 2	DAY 2	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 2	2
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 2	1		DAY 0	DAY 0	1
	Decreased Activity 3	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 3-F
DOSE: 110 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
576	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 1	DAY 1	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Decreased Activity 3	2		DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
577	Second Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
578	Second Clinical Sign			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
579	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 3-F
DOSE: 110 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
580	Second Clinical Sign			DAY 0	DAY 0	1
	Decreased Activity 1	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1
2
3

Slight
Moderate
Severe

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 4-F
DOSE: 250 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
586	First Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
587	First Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
588	Second Clinical Sign			DAY 0	DAY 0	1
	Blue Feet 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
589	First Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
590	First Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP24
DAY 0-DAY 14

GROUP: 5-F
DOSE: 600 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
596	Second Clinical Sign	2		DAY 0	DAY 0	1
	Decreased Activity 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
597	Second Clinical Sign	1		DAY 0	DAY 0	1
	Decreased Activity 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
598	Second Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
599	Second Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
600	Third Clinical Sign	1		DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Decreased Activity 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1
2
3

Slight
Moderate
Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 1-F
DOSE: 5 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
471	Activity Decreased	1		DAY 10	DAY 10	1
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 4	1
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	9
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
472	Activity Decreased	1		DAY 10	DAY 10	1
	Hunched Posture			DAY 11	DAY 13	3
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 6	3
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	9
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
473	Hunched Posture			DAY 1	DAY 11	3
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 8	5
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	8
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
474	Activity Decreased	1		DAY 11	DAY 11	1
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 6	3
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	10
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 1-F
DOSE: 5 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
475	Hunched Posture			DAY 1	DAY 11	3
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 6	3
	Normal 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	10
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 2-F
DOSE: 10(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
461	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 9	3
	Rough Coat			DAY 1	DAY 13	10
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
462	Activity Decreased	1		DAY 10	DAY 11	2
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 5	1
	Rough Coat			DAY 1	DAY 13	9
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
463	Activity Decreased	1		DAY 1	DAY 13	5
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 6	3
	Rough Coat			DAY 1	DAY 9	6
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
464	Activity Decreased	1		DAY 1	DAY 13	6
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 2-F
DOSE: 10 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Normal			DAY 4	DAY 6	3
	Rough Coat			DAY 1	DAY 13	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
465	Activity Decreased	1		DAY 10	DAY 11	2
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 4	DAY 6	3
	Rough Coat			DAY 1	DAY 13	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 3-F
DOSE: 16.5 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
451	Abdomen Bloated	1		DAY 7	DAY 7	1
	Activity Decreased			DAY 11	DAY 11	1
	Hunched Posture			DAY 1	DAY 13	11
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
452	Abdomen Bloated	1		DAY 7	DAY 8	2
	Activity Decreased			DAY 2	DAY 11	3
	Hunched Posture			DAY 1	DAY 13	11
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
453	Hunched Posture			DAY 1	DAY 13	11
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
454	Hunched Posture			DAY 1	DAY 13	9
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 3-F
DOSE: 16.5 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
455	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 5	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
	Abdomen Bloated			DAY 7	DAY 8	2
	Activity Decreased	1		DAY 10	DAY 11	2
	Hunched Posture			DAY 1	DAY 12	10
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 5	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1
2
3

Slight
Moderate
Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 4-F
DOSE: 30(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
441			DAY 2	DAY 2	1
	Abdomen Bloated			DAY 1	DAY 2	2
	Animal Found Dead			DAY 3	DAY 3	1
	Hunched Posture			DAY 1	DAY 2	2
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
442	Abdomen Bloated			DAY 1	DAY 7	7
	Blue Feet			DAY 7	DAY 7	1
	Activity Decreased	1		DAY 2	DAY 2	1
	Animal Found Dead			DAY 7	DAY 7	1
	Hunched Posture			DAY 1	DAY 7	7
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 7	7
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
443	Abdomen Bloated			DAY 1	DAY 9	4
	Activity Decreased	1		DAY 10	DAY 13	3
	Hunched Posture			DAY 1	DAY 13	10
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP4A
DAY 0-DAY 14

GROUP: 4-F
DOSE: 30(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
444	Abdomen Bloated			DAY 1	DAY 9	9
	Blue Feet			DAY 4	DAY 7	4
	Activity Decreased	1		DAY 2	DAY 13	2
	Hunched Posture			DAY 1	DAY 13	13
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 13	13
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
445	Activity Decreased 1	1		DAY 0	DAY 0	1
	Activity Decreased 2	1		DAY 0	DAY 0	1
	Animal Found Dead			DAY 4	DAY 4	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 3	3
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

<u>Severity No.</u>	<u>Description</u>
1	Slight
2	Moderate
3	Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 1-F
DOSE: 550(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
606	Ataxia 3			DAY 0	DAY 0	1
	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 3	DAY 3	1
	Decreased Activity	2		DAY 1	DAY 2	2
	Decreased Activity 3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 4	DAY 4	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Normal			DAY 11	DAY 13	3
	Rough Coat			DAY 1	DAY 10	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
607	Third Clinical Sign			DAY 0	DAY 0	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
608	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 1-F
DOSE: 550 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
609	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose			DAY 1	DAY 1	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
610	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	First Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 2-F
DOSE: 700 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
616	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
617	Second Clinical Sign			DAY 0	DAY 0	1
	Blue Feet 1			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
618	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 3	DAY 4	2
	Decreased Activity	2		DAY 1	DAY 2	2
	Decreased Activity 1	2		DAY 0	DAY 0	1
	Decreased Activity 2	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 11	11
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Normal			DAY 12	DAY 13	2
	Rough Coat			DAY 1	DAY 11	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 2-F
DOSE: 700 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
619	Third Clinical Sign			DAY 0	DAY 0	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
620	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 3-F
DOSE: 900 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
626	Third Clinical Sign			DAY 0	DAY 0	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
627	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
628	Second Clinical Sign			DAY 0	DAY 0	1
	Blue Feet 1			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
629	First Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
630	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 3-F
DOSE: 900 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 4-F
DOSE: 1150 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
636	Ataxia 2			DAY 0	DAY 0	1
	Ataxia 3			DAY 0	DAY 0	1
	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 5	5
	Decreased Activity 1	3		DAY 0	DAY 0	1
	Decreased Activity 3	2		DAY 0	DAY 0	1
	Animal Found Dead			DAY 6	DAY 6	1
	Hunched Posture			DAY 1	DAY 5	5
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 5	5
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
637	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 2	DAY 4	3
	Decreased Activity	2		DAY 1	DAY 1	1
	Decreased Activity 3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 4	DAY 6	3
	Hunched Posture 2			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Normal			DAY 12	DAY 13	2
	Rough Coat			DAY 1	DAY 11	11
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
	Tip of Tail Darkened			DAY 4	DAY 4	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 4-F
DOSE: 1150 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
638	Ataxia	2		DAY 1	DAY 1	1
	Ataxia 2			DAY 0	DAY 0	1
	Ataxia 3			DAY 0	DAY 0	1
	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 2	DAY 5	4
	Decreased Activity	2		DAY 1	DAY 1	1
	Decreased Activity 1	3		DAY 0	DAY 0	1
	Decreased Activity 3	3		DAY 0	DAY 0	1
	Animal Found Dead			DAY 6	DAY 6	1
	Hunched Posture			DAY 1	DAY 5	5
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	End Half of Tail Darkened			DAY 4	DAY 5	2
	Lethargic 2			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 5	5
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Tip of Tail Darkened			DAY 3	DAY 3	1
639	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 4	DAY 4	1
	Decreased Activity	2		DAY 3	DAY 3	1
	Decreased Activity	3		DAY 1	DAY 2	2
	Dark Material Around Eyes			DAY 2	DAY 2	1
	Hunched Posture			DAY 1	DAY 11	9
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 4-F
DOSE: 1150 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Normal			DAY 12	DAY 13	2
	Rough Coat			DAY 1	DAY 11	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
	Tip of Tail Darkened			DAY 4	DAY 4	1
640	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose			DAY 1	DAY 1	1
	Comatose 2			DAY 0	DAY 0	1
	Animal Found Dead			DAY 2	DAY 2	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 5-F
DOSE: 1500 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
646	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
647	First Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
648	Ataxia	1		DAY 1	DAY 2	2
	Blue Feet			DAY 1	DAY 2	2
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	2		DAY 1	DAY 2	2
	Animal Found Dead			DAY 4	DAY 4	1
	Hunched Posture			DAY 1	DAY 2	2
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Lethargic 2			DAY 0	DAY 0	1
	Lethargic 3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 2	2
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
649	First Clinical Sign			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO26
DAY 0-DAY 14

GROUP: 5-F
DOSE: 1500 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
650	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose			DAY 1	DAY 1	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing 1			DAY 0	DAY 0	1
	Labored Breathing 2			DAY 0	DAY 0	1
	Labored Breathing 3			DAY 0	DAY 0	1
	Lethargic 1			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 1-F
DOSE: 150 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
436	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Activity Decreased	1		DAY 1	DAY 10	2
	Activity Decreased 1	1		DAY 0	DAY 0	1
	Activity Decreased 2	1		DAY 0	DAY 0	1
	Activity Decreased 3	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 13	4
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 9	5
	Rough Coat			DAY 1	DAY 13	7
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
437	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Activity Decreased	1		DAY 1	DAY 10	2
	Activity Decreased 1	1		DAY 0	DAY 0	1
	Activity Decreased 2	1		DAY 0	DAY 0	1
	Activity Decreased 3	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 10	2
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 9	5
	Rough Coat			DAY 1	DAY 13	7
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
438	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 1-F
DOSE: 150 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose			DAY 1	DAY 2	2
	Activity Decreased	2		DAY 3	DAY 3	1
	Activity Decreased 1	3		DAY 0	DAY 0	1
	Activity Decreased 2	3		DAY 0	DAY 0	1
	Activity Decreased 3	3		DAY 0	DAY 0	1
	Animal Found Dead			DAY 4	DAY 4	1
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Labored Breathing			DAY 1	DAY 1	1
	Rough Coat			DAY 1	DAY 3	3
	Rough Coat 2			DAY 0	DAY 0	1
439	Blue Feet			DAY 1	DAY 2	2
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Blue Tail			DAY 1	DAY 2	2
	Activity Decreased	1		DAY 2	DAY 3	2
	Activity Decreased	3		DAY 1	DAY 1	1
	Activity Decreased 1	1		DAY 0	DAY 0	1
	Activity Decreased 2	1		DAY 0	DAY 0	1
	Activity Decreased 3	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 13	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 5	DAY 9	4
	Rough Coat			DAY 1	DAY 13	8
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
440	Animal Found Dead			DAY 0	DAY 0	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 2-F
DOSE: 230 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
426	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
427	Blue Feet 1			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
428	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Activity Decreased 1	3		DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Rough Coat 3			DAY 0	DAY 0	1
429	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
430	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 2-F
DOSE: 230 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Animal Found Dead					
	Rough Coat 1					
	Rough Coat 2					
	Rough Coat 3					

DAY 0	DAY 0	1
DAY 0	DAY 0	1
DAY 0	DAY 0	1
DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 3-F
DOSE: 350 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
416	Blue Feet 1			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Rough Coat 1			DAY 0	DAY 0	1
417	Animal Found Dead			DAY 0	DAY 0	1
418	Blue Feet			DAY 1	DAY 3	3
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Blue Tail			DAY 2	DAY 2	1
	Activity Decreased	1		DAY 1	DAY 3	2
	Activity Decreased	2		DAY 2	DAY 2	1
	Activity Decreased 1	1		DAY 0	DAY 0	1
	Activity Decreased 2	1		DAY 0	DAY 0	1
	Activity Decreased 3	2		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 4	4
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 7	DAY 9	3
	Rough Coat			DAY 1	DAY 13	9
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
419	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6A
DAY 0-DAY 14

GROUP: 3-F
DOSE: 350 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
420	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Comatose 1			DAY 0	DAY 0	1
	Comatose 2			DAY 0	DAY 0	1
	Comatose 3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 1-F
DOSE: 40 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
756	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	4
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 6	DAY 13	5
	Rough Coat			DAY 1	DAY 11	7
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
757	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	4
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 10	DAY 13	4
	Rough Coat			DAY 1	DAY 8	8
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
758	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	8
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	5
	Rough Coat			DAY 1	DAY 6	6

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 1-F
DOSE: 40 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
759	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	6
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	4
	Rough Coat			DAY 1	DAY 10	8
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
760	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	5
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	3
	Rough Coat			DAY 1	DAY 11	10
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 2-F
DOSE: 80(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
766	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 1	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	8
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	2
	Rough Coat			DAY 1	DAY 12	11
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
767	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Blue Tail			DAY 1	DAY 1	1
	Decreased Activity	1		DAY 1	DAY 1	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 7	4
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 12	5
	Rough Coat			DAY 1	DAY 13	8
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 2-F
DOSE: 80 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
768	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Blue Tail			DAY 1	DAY 1	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 7	3
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	5
	Rough Coat			DAY 1	DAY 12	8
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
769	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 3	DAY 7	3
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 6	DAY 12	4
	Rough Coat			DAY 1	DAY 13	9
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
770	Blue Feet			DAY 1	DAY 1	1
	Blue Feet 1			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104PO6B
DAY 0-DAY 14

GROUP: 2-F
DOSE: 80(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Blue Feet 2			DAY 0	DAY 0	1
	Blue Feet 3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Decreased Activity	1		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 9	8
	Hunched Posture 1			DAY 0	DAY 0	1
	Hunched Posture 2			DAY 0	DAY 0	1
	Hunched Posture 3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 8	1
	Rough Coat			DAY 1	DAY 13	12
	Rough Coat 1			DAY 0	DAY 0	1
	Rough Coat 2			DAY 0	DAY 0	1
	Rough Coat 3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 1-F
DOSE: 30 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
656	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity #1	1		DAY 0	DAY 0	1
	Decreased Activity #2	3		DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 6	2
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Normal			DAY 8	DAY 13	6
	Rough Coat			DAY 1	DAY 7	6
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
657	Blue Feet			DAY 1	DAY 1	1
	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Lethargic #3			DAY 0	DAY 0	1
	Normal			DAY 3	DAY 13	10
	Rough Coat			DAY 1	DAY 6	3
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
658	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 3	3

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 1-F
DOSE: 30(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 11	DAY 12	2
	Rough Coat			DAY 1	DAY 13	11
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
659	Blue Feet			DAY 1	DAY 1	1
	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 7	DAY 13	6
	Rough Coat			DAY 1	DAY 9	7
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
660	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 1	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 3	DAY 13	11

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 1-F
DOSE: 30 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Rough Coat			DAY 1	DAY 2	2
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 2-F
DOSE: 60(mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
666	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 1	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 3	3
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 13	5
	Rough Coat			DAY 1	DAY 8	7
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
667	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 1	1
	Hunched Posture			DAY 1	DAY 8	5
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Lethargic #3			DAY 0	DAY 0	1
	Normal			DAY 6	DAY 13	3
	Rough Coat			DAY 1	DAY 11	8
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
668	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 1	1

Severity Codes

Severity No.	Description
1	Slight
2	Moderate
3	Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 2-F
DOSE: 60 (mg/kg)

SEX: FEMALE

ANIMAL # OBSERVATIONS SEVERITY LOC ONSET DURATION FREQUENCY

	Hunched Posture			DAY 1	DAY 8	5
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Lethargic #3			DAY 0	DAY 0	1
	Normal			DAY 10	DAY 13	4
	Rough Coat			DAY 1	DAY 9	8
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
669	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 8	5
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Lethargic #2			DAY 0	DAY 0	1
	Lethargic #3			DAY 0	DAY 0	1
	Normal			DAY 3	DAY 12	6
	Rough Coat			DAY 1	DAY 13	7
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1
670	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Decreased Activity	1		DAY 1	DAY 1	1
	Decreased Activity #1	3		DAY 0	DAY 0	1
	Decreased Activity #3	3		DAY 0	DAY 0	1
	Hunched Posture			DAY 1	DAY 12	7
	Hunched Posture #2			DAY 0	DAY 0	1
	Hunched Posture #3			DAY 0	DAY 0	1

Severity Codes

Severity No.

Description

1

Slight

2

Moderate

3

Severe

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 2-F
DOSE: 60 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
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	Lethargic #2			DAY 0	DAY 0	1
	Normal			DAY 9	DAY 13	4
	Rough Coat			DAY 1	DAY 8	8
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Scheduled Sacrifice			DAY 14	DAY 14	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 3-F
DOSE: 125 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
676	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
677	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
678	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 3-F
DOSE: 125 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
679	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
680	Blue Feet			DAY 1	DAY 1	1
	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose			DAY 1	DAY 1	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat			DAY 1	DAY 1	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 4-F
DOSE: 250 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
686	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
687	Blue Feet #1			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
688	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
689	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 4-F
DOSE: 250 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1
690	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 5-F
DOSE: 500 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
696	Blue Feet #1			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
697	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Hunched Posture #1			DAY 0	DAY 0	1
	Hunched Posture #2			DAY 0	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Lethargic #1			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY D	1
698	Blue Feet #1			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
699	Blue Feet #1			DAY 0	DAY 0	1
	Blue Feet #2			DAY 0	DAY 0	1
	Blue Feet #3			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Comatose #2			DAY 0	DAY 0	1
	Comatose #3			DAY 0	DAY 0	1
	Animal Found Dead			DAY 1	DAY 1	1
	Labored Breathing #1			DAY D	DAY 0	1
	Labored Breathing #2			DAY 0	DAY 0	1
	Labored Breathing #3			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1
	Rough Coat #2			DAY 0	DAY 0	1
	Rough Coat #3			DAY 0	DAY 0	1

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL CLINICAL SIGNS

STUDY: 104IP26
DAY 0-DAY 14

GROUP: 5-F
DOSE: 500 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
700	Blue Feet #1			DAY 0	DAY 0	1
	Comatose #1			DAY 0	DAY 0	1
	Animal Found Dead			DAY 0	DAY 0	1
	Labored Breathing #1			DAY 0	DAY 0	1
	Rough Coat #1			DAY 0	DAY 0	1

DRAFT

APPENDIX 4

Individual Body Weights and Body Weight Gains

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 1-M
DOSE: 10 (mg/kg)

SEX: MALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

491	289.2	268.9	307.2	297.1
492	267.0	263.6	319.2	360.7
493	268.7	261.2	319.8	356.2
494	275.8	277.9	340.4	378.1
495	300.4	304.3	383.7	445.8

MEAN	280.2	275.2	334.1	367.6
S.D.	14.27	17.50	30.21	53.32
N	5	5	5	5

--: Data Unavailable

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 2-M

SEX: MALE

DOSE: 15 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

496	270.4	272.7	337.0	381.2
497	272.6	270.2	287.5	339.0
498	281.2	277.7	350.3	485.2
499	291.5	287.0	349.6	401.0
500	258.0	261.3	317.7	354.5

MEAN	274.7	273.8	328.4	392.2
S.D.	12.51	9.48	26.41	57.23
N	5	5	5	5

--: Data Unavailable

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 3-M

SEX: MALE

DOSE: 20 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

501	267.8	265.4	c	c
502	307.5	310.4	c	c
503	286.4	284.4	c	c
504	277.2	278.6	c	c
505	263.7	259.5	c	c

MEAN	280.5	279.7	--	--
S.D.	17.45	19.86	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 4-M
DOSE: 25 (mg/kg)

SEX: MALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

511	294.4	292.9	c	c
512	287.7	290.8	c	c
513	278.8	277.7	c	c
514	268.1	263.7	c	c
515	265.2	267.7	c	c

MEAN	278.8	278.6	--	--
S.D.	12.47	13.18	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 5-M

SEX: MALE

DOSE: 35 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

516	289.3	285.3	c	c
517	300.7	299.7	c	c
518	264.6	264.6	c	c
519	275.6	275.3	c	c
520	271.7	277.4	c	c

MEAN	280.4	280.5	--	--
S.D.	14.49	13.05	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 6-M
DOSE: 50 (mg/kg)

SEX: MALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

521	277.5	271.7	c	c
522	293.4	295.1	c	c
523	272.2	271.1	c	c
524	266.5	264.6	c	c
525	286.3	287.2	c	c

MEAN	279.2	277.9	--	--
S.D.	10.78	12.69	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO4A

GROUP: 1-M
DOSE: 16.5 (mg/kg)

SEX: MALE

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

486	374.7	354.5	c	c
487	387.9	360.0	c	c
488	356.3	338.0	c	c
489	347.4	326.6	345.8	396.1
490	332.9	317.2	325.5	376.4

MEAN	359.8	339.3	335.7	386.3
S.D.	21.80	18.10	14.35	13.93
N	5	5	2	2

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO4A

GROUP: 2-M

SEX: MALE

DOSE: 18.0 (mg/kg)

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

481	360.6	338.3	390.8	438.4
482	324.5	302.5	c	c
483	380.8	361.9	c	c
484	398.3	370.9	c	c
485	354.5	331.4	c	c

MEAN	363.7	341.0	390.8	438.4
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S.D.	27.93	26.98	--	--
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N	5	5	1	1
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--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 1-M

SEX: MALE

DOSE: 20 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

551	282.3	308.2	c	c
552	264.3	291.3	c	c
553	278.0	308.0	c	c
554	297.9	328.7	291.8	352.8
555	270.8	293.3	c	c

MEAN	278.7	305.9	291.8	352.8
S.D.	12.77	15.01	--	--
N	5	5	1	1

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 2-M

SEX: MALE

DOSE: 50 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

561	289.9	306.4	c	c
562	280.0	300.9	c	c
563	298.7	326.3	c	c
564	265.1	286.7	c	c
565	270.0	296.7	c	c

MEAN	280.7	303.4	--	--
S.D.	13.85	14.69	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 3-M

SEX: MALE

DOSE: 110 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

571	280.6	297.0	c	c
572	264.6	292.9	c	c
573	267.7	287.3	c	c
574	285.9	313.6	c	c
575	294.9	317.2	c	c

MEAN	278.7	301.6	--	--
S.D.	12.63	13.12	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 4-M

SEX: MALE

DOSE: 250 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

581	285.1	309.1	298.4	348.2
582	264.5	280.4	c	c
583	276.7	299.8	c	c
584	267.6	290.2	c	c
585	298.9	324.8	c	c

MEAN	278.6	300.9	298.4	348.2
S.D.	13.94	17.13	--	--
N	5	5	1	1

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 5-M

SEX: MALE

DOSE: 600 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

591	268.2	291.0	c	c
592	263.6	288.4	c	c
593	276.4	302.8	c	c
594	289.0	321.9	c	c
595	292.4	316.6	c	c

MEAN	277.9	304.1	--	--
S.D.	12.59	14.94	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP4A

GROUP: 1-M
DOSE: 5 (mg/kg)

SEX: MALE

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

476	409.1	411.1	456.5	509.9
477	333.4	343.9	369.4	410.2
478	350.3	356.8	389.0	421.4
479	371.5	331.2	372.1	404.2
480	356.4	359.9	398.1	434.2

MEAN	364.1	360.6	397.0	436.0
S.D.	28.60	30.45	35.31	42.88
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP4A

GROUP: 2-M

SEX: MALE

DOSE: 10 (mg/kg)

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

466	396.2	405.2	447.3	473.7
467	342.0	356.5	392.4	425.0
468	375.4	378.8	419.9	459.6
469	356.3	366.7	410.0	441.6
470	344.8	351.6	383.0	429.6

MEAN	362.9	371.8	410.5	445.9
S.D.	22.77	21.41	25.13	20.50
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP4A

GROUP: 3-M

SEX: MALE

DOSE: 16.5 (mg/kg)

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

456	355.1	362.7	387.8	423.6
457	340.7	344.0	351.4	399.3
458	369.0	383.8	348.4	366.4
459	356.9	361.4	392.8	439.1
460	407.6	419.6	369.0	c

MEAN	365.9	374.3	369.9	407.1
S.D.	25.40	28.99	20.31	31.69
N	5	5	5	4

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP4A

GROUP: 4-M

SEX: MALE

DOSE: 30 (mg/kg)

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

446	390.4	388.5	384.0	442.5
447	351.5	347.4	c	c
448	382.8	394.1	397.4	448.4
449	360.6	369.6	c	c
450	328.8	334.3	c	c

MEAN	362.8	366.8	390.7	445.5
S.D.	24.75	25.77	9.47	4.17
N	5	5	2	2

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 1-M

SEX: MALE

DOSE: 550 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

601	297.9	303.4	338.9	407.7
602	274.3	287.9	311.2	378.9
603	287.6	287.9	c	c
604	283.3	284.5	c	c
605	264.3	277.2	308.4	379.0

MEAN	281.5	288.2	319.5	388.5
S.D.	12.82	9.57	16.86	16.60
N	5	5	3	3

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 2-M

SEX: MALE

DOSE: 700 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

611	285.8	289.3	312.4	380.3
612	251.1	252.2	279.5	341.3
613	269.6	275.7	c	c
614	282.2	293.5	c	c
615	291.3	305.2	331.9	405.3

MEAN	276.0	283.2	307.9	375.6
S.D.	16.04	20.28	26.48	32.25
N	5	5	3	3

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 3-M
DOSE: 900 (mg/kg)

SEX: MALE

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

621	277.6	250.5	c	c
622	267.2	271.5	c	c
623	273.7	299.7	c	c
624	288.9	304.4	278.7	392.6
625	292.2	304.5	c	c

MEAN	279.9	286.1	278.7	392.6
S.D.	10.46	24.18	--	--
N	5	5	1	1

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

D R A F

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 4-M

SEX: MALE

DOSE: 1150 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

631	281.2	296.8	274.1	370.0
632	289.0	294.9	c	c
633	299.7	308.4	c	c
634	273.2	280.5	c	c
635	262.7	267.2	266.0	340.2

MEAN	281.2	289.6	270.1	355.1
S.D.	14.22	15.95	5.73	21.07
N	5	5	2	2

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 5-M

SEX: MALE

DOSE: 1500 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

641	274.8	284.5	c	c
642	304.6	315.8	c	c
643	287.0	290.8	c	c
644	277.4	287.7	c	c
645	255.5	260.3	c	c

MEAN	279.9	287.8	--	--
S.D.	17.95	19.75	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO6A

GROUP: 2-M

SEX: MALE

DOSE: 230 (mg/kg)

ANIMAL # DAY -2 DAY 7 DAY 14

431	363.9	c	c
432	338.1	328.6	396.5
433	375.5	c	c
434	383.7	413.5	476.3
435	354.4	328.7	405.9

MEAN	363.1	356.9	426.2
S.D.	17.88	48.99	43.61
N	5	3	3

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P06A

GROUP: 3-M

SEX: MALE

DOSE: 350 (mg/kg)

ANIMAL # DAY -2 DAY 7 DAY 14

421	387.3	412.5	468.1
422	356.0	c	c
423	365.7	c	c
424	342.2	c	c
425	317.2	c	c

MEAN	353.7	412.5	468.1
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S.D.	26.19	--	--
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N	5	1	1
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--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO6B

GROUP: 1-M
DOSE: 40 (mg/kg)

SEX: MALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

751	180.4	193.3	267.7	329.7
752	173.9	186.9	272.2	352.1
753	185.0	195.9	282.6	355.7
754	197.8	209.1	285.9	352.2
755	188.9	198.9	279.1	354.3

MEAN	185.2	196.8	277.5	348.8
S.D.	8.99	8.17	7.47	10.78
N	5	5	5	5

--: Data Unavailable

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO6B

GROUP: 2-M

SEX: MALE

DOSE: 80 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

761	178.9	191.8	269.7	341.5
762	184.6	199.0	278.8	359.8
763	201.7	212.0	257.4	293.6
764	171.1	180.7	255.1	330.6
765	194.0	216.9	286.9	349.6

MEAN	186.1	200.1	269.6	335.0
S.D.	12.09	14.75	13.63	25.51
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 1-M

SEX: MALE

DOSE: 30 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

651	260.1	281.0	304.4	338.2
652	253.7	272.2	339.1	390.1
653	251.5	267.8	287.1	329.3
654	277.8	297.2	333.7	408.1
655	238.8	261.1	293.7	347.7

MEAN	256.4	275.9	311.6	362.7
S.D.	14.25	13.95	23.54	34.47
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 2-M

SEX: MALE

DOSE: 60 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

661	258.9	277.0	301.2	347.9
662	244.7	265.8	305.3	361.8
663	281.1	301.3	331.9	382.9
664	242.9	261.0	284.0	319.1
665	264.4	279.2	292.2	345.9

MEAN	258.4	276.9	302.9	351.5
S.D.	15.65	15.63	18.18	23.38
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 3-M

SEX: MALE

DOSE: 125 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

671	252.2	274.3	c	c
672	242.1	260.2	c	c
673	270.4	293.9	344.8	388.4
674	253.8	270.1	298.9	337.8
675	265.4	286.9	c	c

MEAN	256.8	277.1	321.9	363.1
S.D.	11.24	13.42	32.46	35.78
N	5	5	2	2

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 4-M
DOSE: 250 (mg/kg)

SEX: MALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

681	258.5	272.3	c	c
682	250.3	269.8	315.0	376.7
683	228.4	250.7	296.9	343.6
684	268.8	286.8	c	c
685	260.4	276.2	c	c

MEAN	253.3	271.2	306.0	360.2
S.D.	15.38	13.15	12.80	23.41
N	5	5	2	2

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 5-M

SEX: MALE

DOSE: 500 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

691	255.7	276.6	316.3	381.5
692	251.4	269.4	c	c
693	244.1	264.0	c	c
694	268.7	282.4	c	c
695	269.8	286.4	c	c

MEAN	257.9	275.8	316.3	381.5
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S.D.	11.13	9.18	--	--
------	-------	------	----	----

N	5	5	1	1
---	---	---	---	---

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 1-M
DOSE: 10 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
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491	38.3	-10.1	28.2
492	55.6	41.5	97.1
493	58.6	36.4	95.0
494	62.5	37.7	100.2
495	79.4	62.1	141.5

MEAN	58.9	33.5	92.4
S.D.	14.74	26.50	40.69
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 2-M
DOSE: 15 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

496	64.3	44.2	108.5
497	17.3	51.5	68.8
498	72.6	134.9	207.5
499	62.6	51.4	114.0
500	56.4	36.8	93.2

MEAN	54.6	63.8	118.4
S.D.	21.66	40.23	52.80
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 3-M
DOSE: 20 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
501	c	c	--
502	c	c	--
503	c	c	--
504	c	c	--
505	c	c	--
MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 4-M
DOSE: 25 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

511	c	c	--
512	c	c	--
513	c	c	--
514	c	c	--
515	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 5-M
DOSE: 35(mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
516	c	c	--
517	c	c	--
518	c	c	--
519	c	c	--
520	c	c	--
MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 6-M
DOSE: 50 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

521	c	c	--
522	c	c	--
523	c	c	--
524	c	c	--
525	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO4A

GROUP: 1-M
DOSE: 16.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

486	c	c	--
487	c	c	--
488	c	c	--
489	19.2	50.3	69.5
490	8.3	50.9	59.2

MEAN	13.8	50.6	64.4
S.D.	7.71	0.42	7.28
N	2	2	2

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO4A

GROUP: 2-M
DOSE: 18.0 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

481	52.5	47.6	100.1
482	c	c	--
483	c	c	--
484	c	c	--
485	c	c	--

MEAN	52.5	47.6	100.1
S.D.	--	--	--
N	1	1	1

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 1-M
DOSE: 20 (mg/kg)

SEX: MALE

PAGE: 1

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
551	c	c	--
552	c	c	--
553	c	c	--
554	-36.9	61.0	24.1
555	c	c	--
MEAN	-36.9	61.0	24.1
S.D.	--	--	--
N	1	1	1

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 2-M
DOSE: 50 (mg/kg)

SEX: MALE

PAGE: 2

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

561	c	c	--
562	c	c	--
563	c	c	--
564	c	c	--
565	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 3-M
DOSE: 110 (mg/kg)

SEX: MALE

PAGE: 3

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

571	c	c	--
572	c	c	--
573	c	c	--
574	c	c	--
575	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 4-M
DOSE: 250 (mg/kg)

SEX: MALE

PAGE: 4

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
581	-10.7	49.8	39.1
582	c	c	--
583	c	c	--
584	c	c	--
585	c	c	--
MEAN	-10.7	49.8	39.1
S.D.	--	--	--
N	1	1	1

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 5-M
DOSE: 600 (mg/kg)

SEX: MALE

PAGE: 5

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
591	c	c	--
592	c	c	--
593	c	c	--
594	c	c	--
595	c	c	--
MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP4A

GROUP: 1-M
DOSE: 5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

476	45.4	53.4	98.8
477	25.5	40.8	66.3
478	32.2	32.4	64.6
479	40.9	32.1	73.0
480	38.2	36.1	74.3

MEAN	36.4	39.0	75.4
S.D.	7.76	8.81	13.73
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP4A

GROUP: 2-M
DOSE: 10 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

466	42.1	26.4	68.5
467	35.9	32.6	68.5
468	41.1	39.7	80.8
469	43.3	31.6	74.9
470	31.4	46.6	78.0

MEAN	38.8	35.4	74.1
S.D.	4.99	7.86	5.56
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP4A

GROUP: 3-M
DOSE: 16.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

456	25.1	35.8	60.9
457	7.4	47.9	55.3
458	-35.4	18.0	-17.4
459	31.4	46.3	77.7
460	-50.6	c	--

MEAN	-4.4	37.0	44.1
S.D.	36.70	13.76	42.11
N	5	4	4

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP4A

GROUP: 4-M
DOSE: 30 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

446	-4.5	58.5	54.0
447	c	c	--
448	3.3	51.0	54.3
449	c	c	--
450	c	c	--

MEAN	-0.6	54.8	54.2
S.D.	5.52	5.30	0.21
N	2	2	2

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P06B

GROUP: 3-M

SEX: MALE

DOSE: 150 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

771	182.3	189.6	260.7	312.9
772	177.1	192.9	277.8	349.2
773	191.9	191.7	270.4	341.7
774	200.3	209.3	264.8	316.4
775	179.4	189.5	266.1	326.2

MEAN	186.2	194.6	268.0	329.3
S.D.	9.69	8.34	6.50	15.77
N	5	5	5	5

--: Data Unavailable

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P026

GROUP: 1-M
DOSE: 550 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
601	35.5	68.8	104.3
602	23.3	67.7	91.0
603	c	c	--
604	c	c	--
605	31.2	70.6	101.8
MEAN	30.0	69.0	99.0
S.D.	6.19	1.46	7.07
N	3	3	3

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO26

GROUP: 2-M
DOSE: 700(mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

611	23.1	67.9	91.0
612	27.3	61.8	89.1
613	c	c	--
614	c	c	--
615	26.7	73.4	100.1

MEAN	25.7	67.7	93.4
S.D.	2.27	5.80	5.88
N	3	3	3

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO26

GROUP: 3-M
DOSE: 900 (mg/kg)

SEX: MALE

ANIMAL # DAY 7 DAY 14 TOTAL
GAIN

621	c	c	--
622	c	c	--
623	c	c	--
624	-25.7	113.9	88.2
625	c	c	--

MEAN -25.7 113.9 88.2

S.D. -- -- --

N 1 1 1

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO26

GROUP: 4-M
DOSE: 1150 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
631	-22.7	95.9	73.2
632	c	c	--
633	c	c	--
634	c	c	--
635	-1.2	74.2	73.0
MEAN	-12.0	85.1	73.1
S.D.	15.20	15.34	0.14
N	2	2	2

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO26

GROUP: 5-M
DOSE: 1500 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

641	c	c	--
642	c	c	--
643	c	c	--
644	c	c	--
645	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6A

GROUP: 2-M
DOSE: 230 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

431	c	c	--
432	5.5	67.9	73.4
433	c	c	--
434	41.9	62.8	104.7
435	-16.3	77.2	60.9

MEAN	10.4	69.3	79.7
S.D.	29.40	7.30	22.56
N	3	3	3

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6A

GROUP: 3-M
DOSE: 350 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
421	48.0	55.6	103.6
422	c	c	--
423	c	c	--
424	c	c	--
425	c	c	--
MEAN	48.0	55.6	103.6
S.D.	--	--	--
N	1	1	1

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6B

GROUP: 1-M
DOSE: 40 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

751	74.4	62.0	136.4
752	85.3	79.9	165.2
753	86.7	73.1	159.8
754	76.8	66.3	143.1
755	80.2	75.2	155.4

MEAN	80.7	71.3	152.0
S.D.	5.30	7.14	11.93
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6B

GROUP: 2-M
DOSE: 80 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
761	77.9	71.8	149.7
762	79.8	81.0	160.8
763	45.4	36.2	81.6
764	74.4	75.5	149.9
765	70.0	62.7	132.7
MEAN	69.5	65.4	134.9
S.D.	13.98	17.65	31.47
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6B

GROUP: 3-M
DOSE: 150 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
771	71.1	52.2	123.3
772	84.9	71.4	156.3
773	78.7	71.3	150.0
774	55.5	51.6	107.1
775	76.6	60.1	136.7

MEAN	73.4	61.3	134.7
S.D.	11.14	9.75	19.98
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 1-M
DOSE: 30 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
651	23.4	33.8	57.2
652	66.9	51.0	117.9
653	19.3	42.2	61.5
654	36.5	74.4	110.9
655	32.6	54.0	86.6

MEAN	35.7	51.1	86.8
S.D.	18.73	15.25	27.68
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 2-M
DOSE: 60 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
661	24.2	46.7	70.9
662	39.5	56.5	96.0
663	30.6	51.0	81.6
664	23.0	35.1	58.1
665	13.0	53.7	66.7

MEAN	26.1	48.6	74.7
S.D.	9.81	8.37	14.62
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 3-M
DOSE: 125 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

671	c	c	--
672	c	c	--
673	50.9	43.6	94.5
674	28.8	38.9	67.7
675	c	c	--

MEAN	39.9	41.3	81.1
S.D.	15.63	3.32	18.95
N	2	2	2

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 4-M
DOSE: 250 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
681	c	c	--
682	45.2	61.7	106.9
683	46.2	46.7	92.9
684	c	c	--
685	c	c	--
MEAN	45.7	54.2	99.9
S.D.	0.71	10.61	9.90
N	2	2	2

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 5-M
DOSE: 500 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

691	39.7	65.2	104.9
692	c	c	--
693	c	c	--
694	c	c	--
695	c	c	--

MEAN	39.7	65.2	104.9
S.D.	--	--	--
N	1	1	1

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 3-F
DOSE: 20 (mg/kg)

SEX: FEMALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

506	206.1	205.1	234.2	356.0
507	222.7	210.8	233.2	264.8
508	192.3	190.5	229.1	240.4
509	190.0	181.6	195.7	230.5
510	211.1	205.1	232.7	257.5

MEAN	204.4	198.6	225.0	269.8
S.D.	13.57	12.12	16.48	50.04
N	5	5	5	5

--: Data Unavailable

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 6-F

SEX: FEMALE

DOSE: 50 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

526	201.5	197.7	218.2	242.7
527	191.0	188.4	198.1	219.3
528	211.9	201.2	223.9	250.6
529	222.7	215.5	241.6	210.8
530	197.8	198.8	227.8	263.2

MEAN	205.0	200.3	221.9	237.3
S.D.	12.46	9.78	15.87	21.81
N	5	5	5	5

--: Data Unavailable

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

D R A

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 7-F

SEX: FEMALE

DOSE: 110 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

531	216.8	207.2	216.0	249.9
532	181.5	175.8	169.7	227.7
533	209.8	197.5	155.8	c
534	204.8	197.9	c	c
535	200.6	196.3	215.8	240.6

MEAN	202.7	194.9	189.3	239.4
S.D.	13.30	11.55	31.21	11.15
N	5	5	4	3

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 8-F

SEX: FEMALE

DOSE: 250 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

536	219.8	210.0	c	c
537	189.2	189.3	155.7	198.4
538	198.8	189.9	c	c
539	205.3	207.2	c	c
540	207.6	199.8	c	c

MEAN	204.1	199.2	155.7	198.4
S.D.	11.29	9.56	--	--
N	5	5	1	1

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P024

GROUP: 9-F

SEX: FEMALE

DOSE: 600 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

541	227.5	214.7	c	c
542	191.4	188.5	c	c
543	209.9	203.3	c	c
544	206.4	205.5	c	c
545	198.0	201.3	c	c

MEAN	206.6	202.7	--	--
S.D.	13.72	9.43	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 1-F

SEX: FEMALE

DOSE: 20 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

556	195.0	204.1	c	c
557	188.3	204.4	c	c
558	216.5	224.4	215.3	241.4
559	210.8	230.0	c	c
560	206.8	220.7	218.3	263.9

MEAN	203.5	216.7	216.8	252.7
S.D.	11.58	11.86	2.12	15.91
N	5	5	2	2

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 2-F

SEX: FEMALE

DOSE: 50 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

566	213.4	215.4	c	c
567	180.2	195.0	c	c
568	204.8	218.8	c	c
569	217.9	227.6	c	c
570	197.8	205.2	c	c

MEAN	202.8	212.4	--	--
S.D.	14.83	12.61	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 3-F

SEX: FEMALE

DOSE: 110 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

576	219.8	232.6	c	c
577	201.7	210.7	c	c
578	197.4	213.3	c	c
579	180.8	184.4	c	c
580	213.2	215.0	c	c

MEAN	202.6	211.2	--	--
S.D.	15.09	17.29	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 4-F
DOSE: 250 (mg/kg)

SEX: FEMALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

586	204.4	219.3	c	c
587	220.0	228.5	c	c
588	196.8	208.6	c	c
589	187.4	188.5	c	c
590	214.6	229.0	c	c

MEAN	204.6	214.8	--	--
S.D.	13.17	16.88	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP24

GROUP: 5-F

SEX: FEMALE

DOSE: 600 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

596	215.3	221.0	c	c
597	200.8	210.9	c	c
598	193.2	208.8	c	c
599	191.0	195.0	c	c
600	211.7	218.0	c	c

MEAN	202.4	210.7	--	--
S.D.	10.84	10.12	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP4A

GROUP: 1-F
DOSE: 5 (mg/kg)

SEX: FEMALE

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

471	248.7	248.6	262.8	273.2
472	263.3	265.6	270.4	282.2
473	233.5	231.1	250.1	255.0
474	224.6	231.6	244.8	257.3
475	202.9	207.0	224.0	237.2

MEAN	234.6	236.8	250.4	261.0
S.D.	23.07	21.89	17.90	17.42
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP4A

GROUP: 2-F

SEX: FEMALE

DOSE: 10 (mg/kg)

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

461	241.9	234.1	257.7	278.0
462	240.2	239.1	252.0	270.5
463	266.6	268.3	289.2	306.0
464	206.4	211.0	222.1	231.4
465	221.5	215.5	237.2	244.9

MEAN	235.3	233.6	251.6	266.2
S.D.	22.76	22.76	25.14	29.18
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP4A

GROUP: 3-F

SEX: FEMALE

DOSE: 16.5 (mg/kg)

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

451	237.9	239.4	260.8	269.7
452	215.1	212.3	218.2	229.4
453	226.6	231.7	253.8	262.6
454	265.9	262.6	285.2	300.5
455	254.1	253.7	279.9	285.3

MEAN	239.9	239.9	259.6	269.5
S.D.	20.45	19.59	26.54	26.77
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP4A

GROUP: 4-F

SEX: FEMALE

DOSE: 30 (mg/kg)

ANIMAL # DAY -2 DAY 0 DAY 7 DAY 14

441	245.2	244.2	c	c
442	266.0	263.0	211.6	c
443	215.2	207.5	229.9	249.4
444	236.3	234.7	239.6	257.3
445	223.8	230.8	c	c

MEAN 237.3 236.0 227.0 253.4

S.D. 19.73 20.23 14.22 5.59

N 5 5 3 2

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 1-F

SEX: FEMALE

DOSE: 550 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

606	190.0	190.7	207.5	229.5
607	179.8	179.7	c	c
608	209.3	222.5	c	c
609	199.8	208.1	c	c
610	213.3	220.5	c	c

MEAN	198.4	204.3	207.5	229.5
S.D.	13.78	18.70	--	--
N	5	5	1	1

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 2-F

SEX: FEMALE

DOSE: 700 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

616	205.0	207.0	c	c
617	185.4	179.9	c	c
618	197.3	194.1	200.2	232.2
619	215.9	217.6	c	c
620	193.3	192.1	c	c

MEAN	199.4	198.1	200.2	232.2
S.D.	11.63	14.51	--	--
N	5	5	1	1

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 3-F

SEX: FEMALE

DOSE: 900 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

626	208.7	205.5	c	c
627	188.8	187.0	c	c
628	191.5	198.7	c	c
629	198.5	197.4	c	c
630	214.6	208.3	c	c

MEAN	200.4	199.4	--	--
S.D.	11.04	8.29	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 4-F

SEX: FEMALE

DOSE: 1150 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

636	203.9	203.3	c	c
637	219.2	225.7	229.4	282.6
638	196.9	195.5	c	c
639	184.3	186.8	187.3	220.1
640	207.3	214.1	c	c

MEAN	202.3	205.1	208.4	251.4
S.D.	12.91	15.29	29.77	44.19
N	5	5	2	2

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO26

GROUP: 5-F

SEX: FEMALE

DOSE: 1500 (mg/kg)

ANIMAL # DAY -4 DAY 0 DAY 7 DAY 14

646	220.7	224.7	c	c
647	189.3	191.6	c	c
648	210.0	215.0	c	c
649	201.0	199.1	c	c
650	194.8	195.3	c	c

MEAN	203.2	205.1	--	--
S.D.	12.46	14.11	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P06A

GROUP: 1-F

SEX: FEMALE

DOSE: 150 (mg/kg)

ANIMAL # DAY -2 DAY 7 DAY 14

436	243.4	249.1	272.7
437	220.1	235.8	248.2
438	235.6	c	c
439	227.8	252.4	282.7
440	274.5	c	c

MEAN	240.3	245.8	267.9
S.D.	21.01	8.79	17.75
N	5	3	3

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO6A

GROUP: 2-F

SEX: FEMALE

DOSE: 230 (mg/kg)

ANIMAL # DAY -2 DAY 7 DAY 14

426	237.2	c	c
427	245.7	c	c
428	227.8	c	c
429	215.8	c	c
430	269.4	c	c

MEAN 239.2 -- --

S.D. 20.22 -- --

N 5 0 0

--: Data Unavailable

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO6A

GROUP: 3-F

SEX: FEMALE

DOSE: 350 (mg/kg)

ANIMAL # DAY -2 DAY 7 DAY 14

416	241.8	c	c
417	214.3	c	c
418	227.1	224.2	254.0
419	246.4	c	c
420	266.2	c	c

MEAN 239.2 224.2 254.0

S.D. 19.71 -- --

N 5 1 1

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104P06B

GROUP: 1-F

SEX: FEMALE

DOSE: 40 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

756	158.5	160.5	188.2	220.8
757	146.5	148.6	186.0	214.0
758	172.3	174.9	212.3	242.7
759	173.4	174.5	203.5	233.8
760	165.1	171.2	215.5	247.8

MEAN	163.2	165.9	201.1	231.8
S.D.	11.08	11.31	13.54	14.29
N	5	5	5	5

--: Data Unavailable

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104PO6B

GROUP: 2-F

SEX: FEMALE

DOSE: 80 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

766	160.8	160.5	197.1	228.9
767	161.8	166.8	206.7	239.8
768	178.4	188.5	231.3	261.3
769	153.5	165.2	196.0	222.3
770	167.1	169.1	209.7	254.3

MEAN	164.3	170.0	208.2	241.3
S.D.	9.24	10.80	14.23	16.48
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 1-F
DOSE: 30 (mg/kg)

SEX: FEMALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

656	210.9	221.9	252.1	286.6
657	201.5	210.2	230.2	248.0
658	193.4	202.2	212.2	235.8
659	200.5	209.3	223.3	250.0
660	189.2	193.7	226.7	248.4

MEAN	199.1	207.5	228.9	253.8
S.D.	8.33	10.45	14.62	19.22
N	5	5	5	5

---: Data Unavailable

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 2-F
DOSE: 60 (mg/kg)

SEX: FEMALE

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

666	203.4	209.5	252.3	258.0
667	217.4	225.7	248.8	278.8
668	195.9	204.8	226.3	253.8
669	185.3	187.2	212.9	225.2
670	198.7	200.8	221.1	241.3

MEAN	200.1	205.6	232.3	251.4
S.D.	11.71	13.98	17.39	19.93
N	5	5	5	5

--: Data Unavailable

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 3-F

SEX: FEMALE

DOSE: 125 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

676	201.5	211.5	c	c
677	215.2	219.4	c	c
678	190.9	192.7	c	c
679	194.7	196.2	c	c
680	201.1	202.3	c	c

MEAN	200.7	204.4	--	--
S.D.	9.26	11.00	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 4-F

SEX: FEMALE

DOSE: 250 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

686	195.3	202.9	c	c
687	179.1	188.5	c	c
688	201.9	205.2	c	c
689	211.5	220.6	c	c
690	200.1	208.7	c	c

MEAN	197.6	205.2	--	--
S.D.	11.89	11.55	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 104IP26

GROUP: 5-F

SEX: FEMALE

DOSE: 500 (mg/kg)

ANIMAL # DAY -3 DAY 0 DAY 7 DAY 14

696	207.9	215.9	c	c
697	198.7	205.1	c	c
698	194.1	204.5	c	c
699	206.6	217.3	c	c
700	182.8	184.0	c	c

MEAN	198.0	205.4	--	--
S.D.	10.23	13.33	--	--
N	5	5	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 3-F
DOSE: 20 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
506	29.1	121.8	150.9
507	22.4	31.6	54.0
508	38.6	11.3	49.9
509	14.1	34.8	48.9
510	27.6	24.8	52.4
MEAN	26.4	44.9	71.2
S.D.	9.01	43.95	44.59
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 6-F
DOSE: 50 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
526	20.5	24.5	45.0
527	9.7	21.2	30.9
528	22.7	26.7	49.4
529	26.1	-30.8	-4.7
530	29.0	35.4	64.4

MEAN	21.6	15.4	37.0
S.D.	7.40	26.36	26.19
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 7-F
DOSE: 110 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
531	8.8	33.9	42.7
532	-6.1	58.0	51.9
533	-41.7	c	--
534	c	c	--
535	19.5	24.8	44.3
MEAN	-4.9	38.9	46.3
S.D.	26.70	17.16	4.92
N	4	3	3

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 8-F
DOSE: 250 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

536	c	c	--
537	-33.6	42.7	9.1
538	c	c	--
539	c	c	--
540	c	c	--

MEAN	-33.6	42.7	9.1
S.D.	--	--	--
N	1	1	1

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P024

GROUP: 9-F
DOSE: 600 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

541	c	c	--
542	c	c	--
543	c	c	--
544	c	c	--
545	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 1-F
DOSE: 20 (mg/kg)

SEX: FEMALE

PAGE: 6

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
556	c	c	--
557	c	c	--
558	-9.1	26.1	17.0
559	c	c	--
560	-2.4	45.6	43.2
MEAN	-5.8	35.9	30.1
S.D.	4.74	13.79	18.53
N	2	2	2

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 2-F
DOSE: 50 (mg/kg)

SEX: FEMALE

PAGE: 7

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

566	c	c	--
567	c	c	--
568	c	c	--
569	c	c	--
570	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 3-F
DOSE: 110 (mg/kg)

SEX: FEMALE

PAGE: 8

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

576	c	c	--
577	c	c	--
578	c	c	--
579	c	c	--
580	c	c	--

MEAN	--	--	--
------	----	----	----

S.D.	--	--	--
------	----	----	----

N	0	0	0
---	---	---	---

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 4-F
DOSE: 250 (mg/kg)

SEX: FEMALE

PAGE: 9

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

586	c	c	--
587	c	c	--
588	c	c	--
589	c	c	--
590	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP24

GROUP: 5-F
DOSE: 600 (mg/kg)

SEX: FEMALE

PAGE: 10

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
596	c	c	--
597	c	c	--
598	c	c	--
599	c	c	--
600	c	c	--
MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable

c: Animal Found Dead

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP4A

GROUP: 1-F
DOSE: 5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

471	14.2	10.4	24.6
472	4.8	11.8	16.6
473	19.0	4.9	23.9
474	13.2	12.5	25.7
475	17.0	13.2	30.2

MEAN	13.6	10.6	24.2
S.D.	5.45	3.33	4.91
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP4A

GROUP: 2-F
DOSE: 10(mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
461	23.6	20.3	43.9
462	12.9	18.5	31.4
463	20.9	16.8	37.7
464	11.1	9.3	20.4
465	21.7	7.7	29.4
MEAN	18.0	14.5	32.6
S.D.	5.64	5.66	8.86
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP4A

GROUP: 3-F

SEX: FEMALE

DOSE: 16.5 (mg/kg)

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

451	21.4	8.9	30.3
452	5.9	11.2	17.1
453	22.1	8.8	30.9
454	22.6	15.3	37.9
455	26.2	5.4	31.6

MEAN	19.6	9.9	29.6
S.D.	7.90	3.65	7.60
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL TOXICITY STUDY OF
WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP4A

GROUP: 4-F
DOSE: 30 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
441	c	c	--
442	-51.4	c	--
443	22.4	19.5	41.9
444	4.9	17.7	22.6
445	c	c	--
MEAN	-8.0	18.6	32.3
S.D.	38.56	1.27	13.65
N	3	2	2

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P026

GROUP: 1-F
DOSE: 550 (mg/kg)

SEX: FEMALE

ANIMAL # DAY 7 DAY 14 TOTAL
GAIN

606	16.8	22.0	38.8
607	c	c	--
608	c	c	--
609	c	c	--
610	c	c	--

MEAN	16.8	22.0	38.8
S.D.	--	--	--
N	1	1	1

--: Data Unavailable b: Scheduled Sacrifice c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO26

GROUP: 2-F
DOSE: 700 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

616	c	c	--
617	c	c	--
618	6.1	32.0	38.1
619	c	c	--
620	c	c	--

MEAN	6.1	32.0	38.1
------	-----	------	------

S.D.	--	--	--
------	----	----	----

N	1	1	1
---	---	---	---

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO26

GROUP: 3-F
DOSE: 900 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
626	c	c	--
627	c	c	--
628	c	c	--
629	c	c	--
630	c	c	--
MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO26

GROUP: 4-F
DOSE: 1150 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

636	c	c	--
637	3.7	53.2	56.9
638	c	c	--
639	0.5	32.8	33.3
640	c	c	--

MEAN	2.1	43.0	45.1
S.D.	2.26	14.42	16.69
N	2	2	2

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO26

GROUP: 5-F
DOSE: 1500 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

646	c	c	--
647	c	c	--
648	c	c	--
649	c	c	--
650	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6A

GROUP: 1-F
DOSE: 150 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

436	11.5	23.6	35.1
437	22.5	12.4	34.9
438	c	c	--
439	30.3	30.3	60.6
440	c	c	--

MEAN	21.4	22.1	43.5
S.D.	9.45	9.04	14.78
N	3	3	3

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104P06A

GROUP: 2-F
DOSE: 230 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

426	c	c	--
427	c	c	--
428	c	c	--
429	c	c	--
430	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY OF
WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6A

GROUP: 3-F
DOSE: 350 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
416	c	c	--
417	c	c	--
418	1.3	29.8	31.1
419	c	c	--
420	c	c	--

MEAN	1.3	29.8	31.1
S.D.	--	--	--
N	1	1	1

--: Data Unavailable

b: Scheduled Sacrifice

c: Animal Found Dead

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6B

GROUP: 1-F
DOSE: 40 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
756	27.7	32.6	60.3
757	37.4	28.0	65.4
758	37.4	30.4	67.8
759	29.0	30.3	59.3
760	44.3	32.3	76.6
MEAN	35.2	30.7	65.9
S.D.	6.84	1.85	6.95
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE ORAL TOXICITY STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104PO6B

GROUP: 2-F
DOSE: 80 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
766	36.6	31.8	68.4
767	39.9	33.1	73.0
768	42.8	30.0	72.8
769	30.8	26.3	57.1
770	40.6	44.6	85.2

MEAN	38.1	33.2	71.3
S.D.	4.67	6.89	10.10
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 1-F
DOSE: 30 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
656	30.2	34.5	64.7
657	20.0	17.8	37.8
658	10.0	23.6	33.6
659	14.0	26.7	40.7
660	33.0	21.7	54.7
MEAN	21.4	24.9	46.3
S.D.	9.98	6.28	12.98
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 2-F
DOSE: 60 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
666	42.8	5.7	48.5
667	23.1	30.0	53.1
668	21.5	27.5	49.0
669	25.7	12.3	38.0
670	20.3	20.2	40.5
MEAN	26.7	19.1	45.8
S.D.	9.24	10.20	6.32
N	5	5	5

--: Data Unavailable b: Scheduled Sacrifice

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 3-F
DOSE: 125 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

676	c	c	--
677	c	c	--
678	c	c	--
679	c	c	--
680	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 4-F
DOSE: 250 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

686	c	c	--
687	c	c	--
688	c	c	--
689	c	c	--
690	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

ACUTE INTRAPERITONEAL STUDY
OF WR269410 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 104IP26

GROUP: 5-F
DOSE: 500 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7	DAY 14	TOTAL GAIN
----------	-------	--------	---------------

696	c	c	--
697	c	c	--
698	c	c	--
699	c	c	--
700	c	c	--

MEAN	--	--	--
S.D.	--	--	--
N	0	0	0

--: Data Unavailable c: Animal Found Dead

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APPENDIX 5

Individual Necropsy Observations

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

Individual Necropsy Observations

WR242511 Tartrate (Gavage)

(10 mg base/kg)493 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

495 M

SPLEEN - ENLARGED

LIVER - ENLARGED (ENTIRE)

(15 mg base/kg)496 M

LIVER - ALL LOBES ENLARGED

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

497 M

LIVER - ALL LOBES ENLARGED

498 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

499 M

SPLEEN - ENLARGED

LIVER - ALL LOBES ENLARGED

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

500 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

LIVER - ALL LOBES ENLARGED

(16.5 mg base/kg)489 M

KIDNEYS - MULTIPLE IRREGULAR BILATERAL MOTTLED LESIONS

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

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Individual Necropsy Observations

WR242511 Tartrate (Gavage) contd.

(20 mg base/kg)

501 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION

502 M

HEART - ALL CHAMBERS ENLARGED

LIVER - ALL LOBES ENLARGED AND MOTTLED

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

503 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED PIGMENTATION

504 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED PIGMENTATION

505 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED COLOR

507 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

508 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

509 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

(25 mg base/kg)

511 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION

513 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION

514 M

LIVER - ENLARGED WITH YELLOW AND RED MOTTLED PIGMENTATION

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ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

Individual Necropsy Observations

WR242511 Tartrate (Gavage) contd.

(35 mg base/kg)

516 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION
KIDNEY - THICK AND ENLARGED (BOTH)

517 M

LIVER - ENLARGED WITH MOTTLED YELLOW PIGMENTATION

518 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION

520 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION

(50 mg base/kg)

522 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION
KIDNEYS - BOTH ARE ENLARGED THICK AND RAISED
BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

523 M

LIVER - ALL LOBES ENLARGED WITH MOTTLED PIGMENTATION
BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

525 M

LIVER - ALL LOBES ENLARGED AND MOTTLED

(110 mg base/kg)

531 F

SPLEEN - ENLARGED

532 F

SPLEEN - ENLARGED

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR242511 Tartrate (Gavage) contd.

(250 mg base/kg)

536 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

537 F

KIDNEY - MORE THAN 5 YELLOW-WHITE FOCI (LEFT)

SPLEEN - ENLARGED ORGAN

LIVER - ALL LOBES ENLARGED WITH MOTTLED YELLOW PIGMENTATION

538 F

LIVER - ALL LOBES ENLARGED WITH MOTTLED PIGMENTATION

540 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

(600 mg base/kg)

541 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

542 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

543 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

Individual Necropsy Observations

WR242511 Tartrate (Intraperitoneal)

(5 mg base/kg)

476 F

KIDNEYS - MULTIPLE IRREGULAR MOTTLED BILATERAL LESIONS

478 F

KIDNEYS - MULTIPLE IRREGULAR MOTTLED BILATERAL LESIONS

(10 mg base/kg)

463 M

LIVER - ONE IRREGULAR WHITE SCAR ON RIGHT LATERAL LOBE ($\approx 18 \times 6$ MM)

470 F

HEART - RED GELATINOUS FLUID IN PERICARDIAL SAC

(16.5 mg base/kg)

451 M

LIVER - IRREGULAR WHITE SCAR ON RIGHT LATERAL LOBE ($\approx 9 \times 6$ MM)

453 F

LIVER - IRREGULAR WHITE ADHESION ON MEDIAN ($\approx 10 \times 3$ MM IN SIZE)

456 F

LIVER - IRREGULAR WHITE SCAR ON RIGHT LATERAL LOBE ($\approx 18 \times 6$ MM)

458 F

STOMACH - DILATED

(20 mg base/kg)

551 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

LIVER - ENLARGED MOTTLED YELLOW PIGMENTATION ON ALL LOBES

552 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

LIVER - YELLOW PIGMENTATION ON ALL LOBES

ABDOMEN - PALE RED WATERY FLUID IN ABDOMINAL CAVITY (≈ 2 cc)

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR242511 Tartrate (Intraperitoneal) contd.

(20 mg base/kg) contd.

554 F

HEART - ALL CHAMBERS ARE ENLARGED
COLON - ENTIRE LENGTH IS DILATED
CECUM - ENTIRE LENGTH IS DILATED

555 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
ABDOMEN - PALE RED WATERY FLUID IN ABDOMINAL CAVITY (≈2 cc)

556 M

ADRENALS - BOTH ARE ENLARGED
BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

558 M

CECUM - ENTIRE LENGTH IS DILATED
COLON - ENTIRE LENGTH IS DILATED
BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

559 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
ABDOMEN - PALE RED WATERY FLUID IN ABDOMINAL CAVITY (≈2 cc)

560 M

CECUM - ENTIRE LENGTH IS DILATED
COLON - ENTIRE LENGTH IS DILATED
ABDOMEN - CLEAR WATERY FLUID IN ABDOMINAL CAVITY (≈1-2 cc)

(30 mg base/kg)

443 F

LIVER - TWO IRREGULAR ADHESION ON LEFT AND MEDIAN LOBES (10X4 MM)

(50 mg base/kg)

561 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES
ABDOMEN - PALE RED WATERY FLUID IN ABDOMINAL CAVITY (≈2 cc)

562 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES
ABDOMEN - PALE RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR242511 Tartrate (Intraperitoneal) contd.

(50 mg base/kg) contd.

563 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

564 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES

ABDOMEN - PALE RED WATERY FLUID IN ABDOMINAL CAVITY (≈2 cc)

565 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

566 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

ABDOMEN - PALE YELLOW WATERY FLUID IN ABDOMINAL CAVITY (≈2 cc)

567 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

569 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

(110 mg base/kg)

571 F

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES

572 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

573 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

574 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

LIVER - YELLOW IRREGULAR PIGMENTATION ON ALL LOBES

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR242511 Tartrate (Intraperitoneal) contd.

(110 mg base/kg) contd.

576 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

579 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

578 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

579 M

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

(250 mg base/kg)

581 F

SKIN - CIRCULAR HOLE ON ABDOMEN (≈3 CM)

LIVER - ENLARGED METTLE YELLOW PIGMENTATION ON ALL LOBES

SPLEEN - ENLARGED

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

582 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

583 F

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

584 F

LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES

585 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

586 M

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

587 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR242511 Tartrate (Intraperitoneal) contd.

(250 mg base/kg) contd.

588 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

589 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

590 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

(600 mg base/kg)

591 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

592 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

593 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

594 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

595 F

BRAIN - RED FLUID IN CRANIAL CAVITY
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY

596 M

ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY

597 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR242511 Tartrate (Intraperitoneal) contd.

(600 mg base/kg) contd.

598 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

600 M

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY
LIVER - IRREGULAR YELLOW PIGMENTATION ON ALL LOBES
ABDOMEN - RED WATERY FLUID IN ABDOMINAL CAVITY (≈3 cc)

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR269410 (Gavage)

(550 mg/kg)

601 M

KIDNEYS - MULTIPLE BILATERAL IRREGULAR DARK LESIONS
SPLEEN - PUNCTATE ROUND WHITE LESION ON THE CAPSULE

608 F

LUNGS - SEVERAL IRREGULAR BLACK SPOTS ON THE ENTIRE LUNGS (1-2 mm)

(700 mg/kg)

615 M

KIDNEYS - MULTIPLE BILATERAL IRREGULAR DARK LESIONS

(900 mg/kg)

622 M

LIVER - ENLARGED WITH YELLOW MOTTLED PIGMENTATION (ALL LOBES)
BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

(1150 mg/kg)

631 M

KIDNEYS - MULTIPLE BILATERAL IRREGULAR DARK LESIONS

(1500 mg/kg)

645 M

LIVER - MOTTLED YELLOW PIGMENTATION ON ALL LOBES

649 F

LUNGS - SEVERAL IRREGULAR BLACK SPOTS ON ENTIRE AREA (1-2 mm)

650 F

LIVER - MOTTLED PIGMENTATION ON ALL LOBES
ADRENALS - BOTH ADRENALS ENLARGED
BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR269410 (Intraperitoneal)

(30 mg/kg)

651 M

KIDNEY - IRREGULAR THIN WHITE LINE ON LEFT CAPSULE (\approx 1 CM)
LIVER - WHITE SCAR TISSUE ON LEFT LATERAL LOBE
SPLEEN - WHITE SCAR TISSUE ON CAPSULE

652 M

KIDNEYS - IRREGULAR RED PIGMENTATION (3-4 PLACES, \approx 1 CM)

653 M

LIVER - ADHESION AND SCAR TISSUE ON ALL LOBES OF THE LIVER

654 M

SPLEEN - WHITE SCAR TISSUE ON CAPSULE

655 M

LIVER - IRREGULAR DEFORMITY ON LEFT LATERAL LOBE
SPLEEN - WHITE SCAR TISSUE ON CAPSULE
KIDNEYS - NUMEROUS SPOTS OF RED PIGMENTATION (\approx 1 CM)

657 F

LIVER - LEFT LATERAL LOBE DEFORMED (IRREGULAR AND THICK)
SPLEEN - WHITE SCAR TISSUE ON CAPSULE

658 F

SPLEEN - ENLARGED AND SCARRED

659 F

SPLEEN - WHITE SCAR TISSUE ON CAPSULE (\approx 1 CM)
LIVER - THICK ROUNDED ADHESION ON ALL LOBES

660 F

KIDNEY - WHITE SCAR TISSUE (LEFT)
SPLEEN - CAPSULE ENLARGED AND ADHERED TO STOMACH WITH SCAR TISSUE
LIVER - ALL LOBES HAVE ADHESIONS AND LEFT LATERAL AND MEDIAN LOBES
ARE ENLARGED AND THICK

(60 mg/kg)

661 M

LIVER - LEFT LATERAL LOBE IS THICK AND IRREGULAR IN SHAPE
SPLEEN - WHITE SCAR TISSUE ON CAPSULE

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR269410 (Intraperitoneal) contd.

(60 mg/kg) contd.

662 M

KIDNEYS - NUMEROUS SPOTS OF IRREGULAR RED PIGMENTATION ($\approx 1/2$ CM)
HEART - ENLARGED
BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

663 M

LIVER - LARGE, THICK AND ROUNDED LEFT LATERAL LOBE
SPLEEN - WHITE SCAR TISSUE ON CAPSULE
HEART - ENLARGED

664 M

LIVER - ADHESION ON ALL LOBES AND LEFT LATERAL LOBE IS DEFORMED
(ROUND) AND ALSO HAS SCAR TISSUE
SPLEEN - SCAR TISSUE ON CAPSULE

665 M

SPLEEN - WHITE SCAR TISSUE ON CAPSULE
LIVER - DEFORMED AND HAS WHITE ADHESION ON ALL LOBES

666 F

KIDNEYS - IRREGULAR RED PIGMENTATIONS ON RIGHT KIDNEY (≈ 1 CM)
LIVER - MEDIAL LEFT LATERAL LOBE IS DEFORMED (IRREGULAR AND THICK) AND
HAS ADHESION
SPLEEN - WHITE SCAR TISSUE ON CAPSULE

667 F

HEART - ENLARGED
SPLEEN - WHITE SCAR TISSUE ON CAPSULE

668 F

SPLEEN - CAPSULE IS ENLARGED AND HAS SCAR TISSUE
BRAIN - GELATINOUS FLUID IN CRANIAL CAVITY

669 F

LIVER - LEFT ANTERIOR AND LEFT LATERAL LOBES ARE DEFORMED
(IRREGULAR AND THICK)
SPLEEN - WHITE SCAR TISSUE ON CAPSULE

670 F

SPLEEN - ENLARGED

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR269410 (Intraperitoneal) contd.

(125 mg/kg)

671 M

LUNGS - TAN IN COLOR

672 M

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY
TESTES - RIGHT TESTICLE IS DARK RED

675 M

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY
LUNGS - ALL LOBES ARE TAN IN COLOR

677 F

LUNGS - ALL LOBES ARE TAN TO DARK BROWN IN COLOR

678 F

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY
LUNGS - ALL LOBES ARE TAN TO DARK BROWN IN COLOR

679 F

BRAIN - RED GELATINOUS FLUID IN CRANIAL CAVITY

680 F

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY
LUNGS - ALL LOBES ARE TAN IN COLOR

(250 mg/kg)

681 M

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY.

682 M

SPLEEN - ENLARGED

683 M

SPLEEN - ENLARGED

684 M

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR269410 (Intraperitoneal) contd. 686 F

(250 mg/kg) contd.

685 M

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY
BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY
LUNGS - ALL LOBES TAN TO DARK BROWN IN COLOR

687 F

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY
LUNGS - ALL LOBES ARE TAN TO DARK BROWN IN COLOR
ABDOMEN - CLOUDY WATER-LIKE FLUID IN THE ABDOMINAL CAVITY (≈2.5 ml)

688 F

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

689 F

ABDOMEN - CLEAR WATER-LIKE FLUID IN THE ABDOMINAL CAVITY (≈0.5 ml)
BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

690 F

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

(500 mg/kg)

692 M

LUNGS - ALL LOBES TAN TO DARK BROWN IN COLOR
ABDOMEN - CLOUDY WATER-LIKE FLUID IN THE ABDOMINAL CAVITY (≈1-2 ml)

693 M

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

694 M

ABDOMEN - CLOUDY WATER-LIKE FLUID IN THE ABDOMINAL CAVITY (≈2.5 ml)
LUNGS - ALL LOBES ARE TAN TO DARK BROWN IN COLOR
BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

695 M

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

696 F

ABDOMEN - CLOUDY WATER-LIKE FLUID IN THE ABDOMINAL CAVITY (≈1.5 ml)
LUNGS - ALL LOBES ARE TAN TO DARK BROWN IN COLOR
BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

698 F

ABDOMEN - CLOUDY WATER-LIKE FLUID IN THE ABDOMINAL CAVITY (≈2 ml)
LUNGS - ALL LOBES ARE TAN TO DARK BROWN IN COLOR

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

Individual Necropsy Observations

WR269410 (Intraperitoneal) contd.

(500 mg/kg) contd.

699 F

BRAIN - RED GELATINOUS FLUID IN THE CRANIAL CAVITY

700 F

ABDOMEN - REDDISH-WHITE CLOUDY LIQUID IN ABDOMINAL CAVITY (≈2 ml)
BRAIN- RED GELATINOUS FLUID IN THE CRANIAL CAVITY

DRAFT

APPENDIX 6

LD50 Data

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

LD50 Data

WR242511 Tartrate (Gavage - Males)

DRAFT

<46> Litchfield & Wilcoxon I: Confidence Limits of ED50
Pharmacologic Calculation System - Version 4.2(C) - 09-03-1993

File name:	WR24POM			
Variable:	Dose	# Responding	# in Group	
# 1:	10	0	5	
# 2:	15	0	5	
# 3:	16.5	3	5	
# 4:	18	4	5	
# 5:	20	5	5	
# 6:	25	5	5	
# 7:	35	5	5	
# 8:	50	5	5	

Observed probit : 5.252934 5.841457

(1) Probit = 15.56985 * Log(Dose) -13.70303

Probit from line : 1.866821 4.608538 5.253016 5.841377 6.553815 8.06269
10.33788 12.74968

Expected effect : 1 34.7832 60.00098 80.00293 93.97559 99 99 99

Obs./Corrected % : .3 9.2 60 80 98 99.7 99.7 99.7

(2) Probit = 8.268903 * Log(Dose) -5.032327

Corrected probit : 2.251845 3.671254 5.252934 5.841457 7.054189 7.748153
7.748153 7.748153

Corrected probit : 3.236576 4.692657 5.03493 5.347399 5.725764 6.527103
7.735422 9.016291

Expected effect : 3.89502 37.94141 51.43555 63.58984 76.60547 93.66455
99 99

Chi-square: 3.452606E-02 .3508331 2.936415E-02 .1163095 .2554062
6.138554E-02 4.949452E-03 4.949452E-03

Slope Function = 1.319076			
Dose	Log(Dose)	% Response	(2) Probit
10	1	.3	2.251845
15	1.176091	9.2	3.671254
16.5	1.217484	60	5.252934
18	1.255273	80	5.841457
20	1.30103	98	7.054189
25	1.39794	99.7	7.748153
35	1.544068	99.7	7.748153
50	1.69897	99.7	7.748153

Total number of animals used = 40
Animals between ED16 & ED84 = 20

Chi-Square for 6 d.f. = 12.592
Chi-Square, calculated = 4.288617

Factor(ED50) = 1.187118

WR24PCM	Value	95% Limits:	Lower C.L.	Upper C.L.
ED50	16.34029		13.76467	19.39786
Log(ED50)	1.21326		1.138766	1.287754

DRAFT

LD50 Data

WR242511 Tartrate (Gavage - Females)

<46> Litchfield & Wilcoxon I: Confidence Limits of ED50
Pharmacologic Calculation System - Version 4.2(C) - 09-03-1993

File name:	WR24POF		
Variable:	Dose	# Responding	# in Group
# 1:	20	0	5
# 2:	50	0	5
# 3:	110	2	5
# 4:	250	4	5
# 5:	600	5	5

Observed probit : 4.747066 5.841457

(1) Probit = 3.069424 * Log(Dose) -1.518836

Probit from line : 2.474577 3.696023 4.747065 5.841459 7.008489

Expected effect : 1 9.613281 39.99902 80.00293 97.76782

Obs./Corrected % : .3 3.2 40 80 99.3

(2) Probit = 3.581964 * Log(Dose) -2.630639

Corrected probit : 2.251845 3.147406 4.747066 5.841457 7.457689

Corrected probit : 2.029603 3.45501 4.681556 5.958695 7.320598

Expected effect : 1 6.120117 37.46289 83.11328 98.98206

Chi-square: 4.949495E-03 1.484117E-02 2.74751E-03 6.905911E-03
1.003298E-03

Slope Function = 1.895139			
Dose	Log(Dose)	% Response	(2) Probit
20	1.30103	.3	2.251845
50	1.69897	3.2	3.147406
110	2.041393	40	4.747066
250	2.39794	80	5.841457
600.0001	2.778151	99.3	7.457689

Total number of animals used = 25
Animals between ED16 & ED84 = 10

Chi-Square for 3 d.f. = 7.815
Chi-Square, calculated = .152237

Factor(ED50) = 1.750652

WR24POF	Value	95% Limits:	Lower C.L.	Upper C.L.
ED50	134.9879		77.10719	236.3168
Log(ED50)	2.130295		1.887095	2.373495

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

LD50 Data

WR242511 Tartrate (Intraperitoneal - Males)

DRAFT

<46> Litchfield & Wilcoxon I: Confidence Limits of ED50
Pharmacologic Calculation System - Version 4.2(C) - 09-10-1993

File name:	104IP24M		
Variable:	Dose	# Responding	# in Group
# 1:	5	0	5
# 2:	10	0	5
# 3:	16.5	1	5
# 4:	20	4	5
# 5:	30	3	5
# 6:	50	5	5
# 7:	110	5	5
# 8:	250	5	5
# 9:	600	5	5

Observed probit : 4.158543 5.841457 5.252934

(1) Probit = 3.046653 * Log(Dose) + 1.026539

Probit from line : 3.156058 4.073192 4.73579 4.990326 5.526815 6.202711
7.245955 8.332231 9.490602

Expected effect : 3.260986 17.7002 39.56836 49.61719 70.09766 88.54443
98.76074 99 99

Obs./Corrected % : 1 5.5 20 80 60 96.5 99.7 99.7 99.7

(2) Probit = 2.678338 * Log(Dose) + 1.361227

Corrected probit : 2.673215 3.401466 4.158543 5.841457 5.252934 6.812316
7.748153 7.748153 7.748153

Corrected probit : 3.233305 4.039565 4.62206 4.845825 5.317456 5.911642
6.828766 7.78372 8.802054

Expected effect : 3.871094 16.83887 35.26172 43.875 62.44141 81.91699
96.63135 99 99

Chi-square: .0221517 9.181341E-02 .1020334 .529959 2.541547E-03 .1435653
2.892813E-02 4.949452E-03 4.949452E-03

Slope Function = 2.351324			
Dose	Log(Dose)	% Response	(2) Probit
5	.69897	1	2.673215
10	1	5.5	3.401466
16.5	1.217484	20	4.158543
20	1.30103	80	5.841457
30	1.477121	60	5.252934
50	1.69897	96.5	6.812316
110	2.041393	99.7	7.748153
250	2.39794	99.7	7.748153
600.0001	2.778151	99.7	7.748153

Total number of animals used = 45
Animals between ED16 & ED84 = 25

Chi-Square for 7 d.f. = 14.067
Chi-Square, calculated = 4.654457

Factor(ED50) = 1.605858

104IP24M	Value	95% Limits:	Lower C.L.	Upper C.L.
ED50	22.83462		14.21958	36.66916
Log(ED50)	1.358594		1.152887	1.564301

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

LD50 Data

WR242511 Tartrate (Intraperitoneal - Females)

DRAFT

<46> Litchfield & Wilcoxon I: Confidence Limits of ED50
Pharmacologic Calculation System - Version 4.2(C) - 09-03-1993

File name:	WR24IPF		
Variable:	Dose	# Responding	# in Group
# 1:	5	0	5
# 2:	10	0	5
# 3:	16.5	0	5
# 4:	20	3	5
# 5:	30	3	5
# 6:	50	5	5
# 7:	110	5	5
# 8:	250	5	5
# 9:	600	5	5

Observed probit : 5.252934 5.252934

(1) Probit = -1.895652E-06 * Log(Dose) + 5.252936

Probit from line : 5.252935 5.252934 5.252934 5.252934 5.252934 5.252933

5.252933 5.252932 5.252931

Expected effect : 60.00098 60.00098 60.00098 60.00098 60.00098 60.00098

60.00098 60.00098 60.00098

Obs./Corrected % : 10.5 10.5 10.5 60 60 90.1 90.1 90.1 90.1

(2) Probit = 1.494383 * Log(Dose) + 2.784443

Corrected probit : 3.746275 3.746275 3.746275 5.252934 5.252934 6.287451

6.287451 6.287451 6.287451

Corrected probit : 3.828972 4.278826 4.60383 4.72868 4.991827 5.323355

5.835065 6.367883 6.936064

Expected effect : 12.07764 23.53809 34.5918 39.28125 49.71289 62.72852

79.81152 91.43945 97.34912

Chi-square: 2.343866E-03 9.445205E-02 .256527 .1799778 4.233124E-02

.3204461 6.569508E-02 2.292033E-03 .2036334

Slope Function = 4.629054

Dose	Log(Dose)	% Response	(2) Probit
5	.69897	10.5	3.746275
10	1	10.5	3.746275
16.5	1.217484	10.5	3.746275
20	1.30103	60	5.252934
30	1.477121	60	5.252934
50	1.69897	90.1	6.287451
110	2.041393	90.1	6.287451
250	2.39794	90.1	6.287451
600.0001	2.778151	90.1	6.287451

Total number of animals used = 45

Animals between ED16 & ED84 = 30

Chi-Square for 7 d.f. = 14.067

Chi-Square, calculated = 5.838492

Factor(ED50) = 2.1705

WR24IPF	Value	95% Limits:	Lower C.L.	Upper C.L.
ED50	30.38015		13.99685	65.94011
Log(ED50)	1.48259		1.14603	1.81915

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

LD50 Data

WR269410 (Gavage - Males)

DRAFT

<46> Litchfield & Wilcoxon I: Confidence Limits of ED50
Pharmacologic Calculation System - Version 4.2(C) - 09-10-1993

File name:	104PO26M		
Variable:	Dose	# Responding	# in Group
# 1:	40	0	5
# 2:	80	0	5
# 3:	150	0	5
# 4:	230	2	5
# 5:	350	4	5
# 6:	550	2	5
# 7:	700	2	5
# 8:	900	4	5
# 9:	1150	3	5
# 10:	1500	5	5

Observed probit : 4.747066 5.841457 4.747066 4.747066 5.841457 5.252934

(1) Probit = .4479395 * Log(Dose) + 3.963878

Probit from line : 4.681504 4.816348 4.938635 5.02179 5.103467 5.191395
5.23831 5.2872 5.334886 5.386575

Expected effect : 37.46289 42.72656 47.51172 50.86133 54.11523 57.6084
59.42676 61.29297 63.11133 65.07324

Obs./Corrected % : 9.4 10.2 10.4 40 80 40 40 80 60 90.8

(2) Probit = 1.540565 * Log(Dose) + .9585255

Corrected probit : 3.683282 3.729592 3.740753 4.747066 5.841457 4.747066
4.747066 5.841457 5.252934 6.328746

Corrected probit : 3.426603 3.890359 4.310935 4.596921 4.877828 5.180233
5.341584 5.509728 5.673729 5.851501

Expected effect : 5.785156 13.3457 24.54297 34.30469 45.11914 57.17773
63.39844 69.52344 74.97852 80.29004

Chi-square: 2.397422E-02 8.556654E-03 .1080076 1.439287E-02 .4913519
.1205134 .2359367 5.180127E-02 .119588 6.979994E-02

Slope Function = 4.421223

Dose	Log(Dose)	% Response	(2) Probit
40	1.60206	9.4	3.683282
80	1.90309	10.2	3.729592
150	2.176091	10.4	3.740753
230.0001	2.361728	40	4.747066
350	2.544068	80	5.841457
549.9999	2.740363	40	4.747066
699.9999	2.845098	40	4.747066
899.9999	2.954242	80	5.841457
1150	3.060698	60	5.252934
1500	3.176091	90.8	6.328746

Total number of animals used = 50
Animals between ED16 & ED84 = 40

Chi-Square for 8 d.f. = 15.507
Chi-Square, calculated = 6.219613

Factor(ED50) = 1.917484

104PO26M	Value	95% Limits:	Lower C.L.	Upper C.L.
ED50	420.1183		219.0987	805.5701

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

DRAFT

LD50 Data

WR269410 (Gavage - Females)

<46> Litchfield & Wilcoxon I: Confidence Limits of ED50
Pharmacologic Calculation System - Version 4.2(C) - 09-03-1993

File name:	WR26POF		
Variable:	Dose	# Responding	# in Group
# 1:	40	0	5
# 2:	80	2	5
# 3:	150	2	5
# 4:	230	5	5
# 5:	350	4	5
# 6:	550	4	5
# 7:	700	4	5
# 8:	900	5	5
# 9:	1150	3	5
# 10:	1500	5	5

Observed probit : 4.747066 4.747066 5.841457 5.841457 5.841457 5.252934

(1) Probit = .8515759 * Log(Dose) + 3.211396

Probit from line : 4.575672 4.832022 5.064503 5.222587 5.377863 5.545023
5.634213 5.727158 5.817813 5.916079

Expected effect : 33.53906 43.30078 52.58398 58.80469 64.73828 70.71973
73.73438 76.65332 79.33301 82.0127

Obs./Corrected % : 9 40 40 90 80 80 80 93.3 60 94.5

(2) Probit = 1.440257 * Log(Dose) + 1.877953

Corrected probit : 3.659031 4.747066 4.747066 6.281729 5.841457 5.841457
5.841457 6.498811 5.252934 6.598534

Corrected probit : 4.185331 4.618892 5.012084 5.279449 5.542066 5.82478
5.975626 6.132823 6.286146 6.452342

Expected effect : 20.7627 35.16602 50.47852 61.00586 70.62402 79.52441
83.54395 87.13281 90.07568 92.68359

Chi-square: 8.410084E-02 1.024907E-02 4.392374E-02 .3533862 .0423729
1.389061E-04 9.135521E-03 3.392418E-02 1.011866 4.865475E-03

Slope Function =	4.903449		
Dose	Log(Dose)	% Response	(2) Probit
40	1.60206	9	3.659031
80	1.90309	40	4.747066
150	2.176091	40	4.747066
230.0001	2.361728	90	6.281729
350	2.544068	80	5.841457
549.9999	2.740363	80	5.841457
699.9999	2.845098	80	5.841457
899.9999	2.954242	93.3	6.498811
1150	3.060698	60	5.252934
1500	3.176091	94.5	6.598534

Total number of animals used = 50
Animals between ED16 & ED84 = 35

Chi-Square for 8 d.f. = 15.507
Chi-Square, calculated = 7.969812

Factor(ED50) = 2.105249

WR26POF	Value	95% Limits:	Lower C.L.	Upper C.L.
ED50	147.1298		69.88713	309.745
Log(ED50)	2.167701		1.844397	2.491004

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN RATS

LD50 Data

WR269410 (Intraperitoneal - Males)

DRAFT

<46> Litchfield & Wilcoxon I: Confidence Limits of ED50
Pharmacologic Calculation System - Version 4.2(C) - 09-03-1993

File name:	WR26IPM			
Variable:	Dose	# Responding	# in Group	
# 1:	30	0	5	
# 2:	60	0	5	
# 3:	125	3	5	
# 4:	250	3	5	
# 5:	500	4	5	

Observed probit : 5.252934 5.252934 5.841457

(1) Probit = .9775007 * Log(Dose) + 3.10512

Probit from line : 4.549007 4.843264 5.154851 5.449108 5.743365

Expected effect : 32.58203 43.7793 56.17285 67.32227 77.13184

Obs./Corrected % : 8.8 10.3 60 60 80

(2) Probit = 1.934523 * Log(Dose) + .7030232

Corrected probit : 3.646605 3.735193 5.252934 5.252934 5.841457

Corrected probit : 3.560548 4.142897 4.759543 5.341892 5.924242

Expected effect : 7.507813 19.56641 40.47754 63.39844 82.25195

Chi-square: 2.404544E-03 5.455997E-02 .1581882 4.977146E-03 3.473937E-03

Slope Function = 3.266483

Dose	Log(Dose)	% Response	(2) Probit
30	1.477121	8.8	3.646605
60	1.778151	10.3	3.735193
125	2.09691	60	5.252934
250	2.39794	60	5.252934
500.0001	2.69897	80	5.841457

Total number of animals used = 25

Animals between ED16 & ED84 = 20

Chi-Square for 3 d.f. = 7.815

Chi-Square, calculated = 1.118019

Factor(ED50) = 2.081693

WR26IPM	Value	95% Limits:	Lower C.L.	Upper C.L.
ED50	166.4209		79.94498	346.4372
Log(ED50)	2.221208		1.902791	2.539624

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APPENDIX 7

Protocol and Amendments

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Contract No.: DAMD17-92-2001
Task Order No.: UIC-7B
UIC/TRL Study No.: 104

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 and WR269410 IN RATS

1.0 PURPOSE OF THE STUDY:

The purpose of this study is to assess the toxicity of the test articles in CD® rats following either a single oral or intraperitoneal dose.

2.0 SPONSOR:

2.1 Name: U.S. Army Medical Research
and Development Command

2.2 Address: Fort Detrick
Frederick, MD 21702-5009

2.3 Representative: George Schieferstein, Ph.D.

3.0 TESTING FACILITY:

3.1 Name: Toxicology Research Laboratory (TRL)

3.2 Address: University of Illinois at Chicago (UIC)
Department of Pharmacology
P.O. Box 6998
Chicago, Illinois 60680

3.3 Study Director: Barry S. Levine, D.Sc., D.A.B.T.

4.0 DATES:

4.1 Study Initiation (see Section 12.0):

12/3/92

4.2 Proposed Initiation of Dosing:

To be determined.

4.3 Proposed Necropsy Date:

14 days after dosing
(the specific date to be
determined later).

4.4 Proposed Study Completion (Final Report): 6 weeks after sacrifice
(the specific date to be
determined later).

5.0 TEST ARTICLES

5A.1 Name or Code No: WR242511 Tartrate
Bottle number will be identified in the raw data.

5A.2 TRL Chemical No: 0930614

5A.3 Physical Description: Orange powder

5A.4 Stability and Handling of Test Article:

5A.4.1 Storage Conditions to Maintain Stability:

5A.4.1.1 Temperature: -20 to -15°C.

5A.4.1.2 Humidity: Ambient conditions at
-20 to -15°C in a
freezer.

5A.4.1.3 Light: Protect from light.

5A.4.1.4 Special Requirements: None.

5A.4.2 Special Handling Procedures: Standard safety
precautions including gloves, labcoat and eye
protection.

5A.4.3 Log of Test Article: The amount, date, identity of
person(s) removing aliquots and the purpose for which
each aliquot of the test article was removed from the
batch will be documented. At termination of the study,
all unused test article will be returned to the Sponsor.

5B.1 Name or Code No: WR269410 (p-Aminoheptanophenone; PAHP)
Bottle number will be identified in the raw
data.

5B.2 TRL Chemical No: 1620614

5B.3 Physical Description: White powder

5B.4 Stability and Handling of Test Article:

5B.4.1 Storage Conditions to Maintain Stability:

5B.4.1.1 Temperature: -20 to -15°C.

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- 5B.4.1.2 Humidity: Ambient conditions at -20 to -15° in a freezer.
- 5B.4.1.3 Light: Protect from light.
- 5B.4.1.4 Special Requirements: None
- 5B.4.2 Special Handling Procedures: Standard precautions including gloves, labcoat and eye protection.
- 5B.4.3 Log of Test Article: The amount, date, identity of person(s) removing aliquots and the purpose for which each aliquot of the test article was removed from the batch will be documented. At termination of the study, all unused test article will be returned to the Sponsor.

6.0 PERSONNEL:

Study Director	Barry S. Levine, D.Sc., D.A.B.T.
Toxicologist	E. Marianna Furedi-Machacek, D.V.M.
Analytical Chemist	Ian R. Tebbett, Ph.D.
Clinical Veterinarian	James Artwohl, D.V.M., M.S., D.A.C.L.A.M.
Veterinary Support	To be documented in the raw data.
Tox. Lab Supervisor	Soudabeh Soura, B.S.
Lead Technician	Nancy Dinger, B.S.
Chemistry Specialist	Thomas Tolhurst, B.S.
Quality Assurance	Ronald C. Schoenbeck

7.0 TEST SYSTEM:

- 7.1 Species: Rat
- 7.2 Strain: CD® (Virus Antibody Free)
- 7.3 Sex(s) and Number: 100 males and 100 females for LD50 test. Up to 20/sex for the range-finding test.
- 7.4 Age of Animals: The animals will be approximately 7 weeks old on the day of dosing.
- 7.5 Weight of Animals: Approximately 200 - 250 g (males) and ≈ 130 - 170 g (females) at dosing.
- 7.6 Source of Animals: Charles River Breeding Laboratories. The specific source will be specified in the raw data.

- 7.7 Justification for Selection of Test System: The rat is a standard and accepted species for toxicology studies, and it is specified by the Sponsor.
- 7.8 Procedure for Unique Identification of Test System: Upon arrival, each animal will be given a study-unique quarantine/pretest number. During the test animal selection process, each test animal will be assigned a test animal number unique to it within the population making up the study. This number will appear as an ear tag and will also appear on a cage card visible on the front of each cage. The cage card will additionally contain the study number, test article identification, treatment group number, and dose level. Cage cards will be color-coded as a function of treatment group. Raw data records and specimens will also be identified by the unique test animal number.
- 7.9 Housing: The animals will be housed in an AAALAC-accredited facility. Animals will be singly housed in polycarbonate cages with Anderson bed-a-cob bedding (Heinold Co., Kankakee, Illinois) in a temperature (65-78°F) and humidity (40-70%) controlled room with a 14 hour light/10 hour dark cycle. The cage size, 840 cm squared area and 20 cm height, is adequate to house rats at the upper weight range as described in the Guide for the Care and Use of Laboratory Animals, DHEW,(NIH) No. 86.23. All animals will be routinely transferred to clean cages with fresh bedding once weekly.
- 7.10 Quarantine Procedure: Animals for the LD50 test will be quarantined for approximately one week. The range-finding test will initiated before the end of the quarantine period. During quarantine, the animals will be observed daily for signs of illness or death and all unusual observations will be reported to the Study Director, Toxicologist or Clinical Veterinarian. Animals will be examined during quarantine and approved for use by the Clinical Veterinarian prior to being placed on test. Any sickly animal will be either eliminated prior to the test animal selection process or replaced by a healthy animal following this procedure but prior to initiation of treatment under the direction of the Study Director or Toxicologist. Quarantine release will be documented on the Clinical Veterinarian Log by a veterinarian prior to study initiation.
- 7.11 Food: Purina Certified Rodent Chow No. 5002 (Ralston Purina Company, St. Louis, MO) will be provided *ad libitum* from arrival until termination, except during an approximate 16-20 hour fast prior to dosing.
- 7.12 Water: Tap water from an automatic watering system in which the distribution lines are flushed daily will be provided *ad libitum* from arrival until termination. The water is untreated with additional chlorine or HCl.

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7.13 There are no known contaminants in the feed or water which are expected to influence the study. A copy of the feed certification will be kept with the study records. The results of the most current comprehensive chemical analyses of Chicago water are documented in files maintained by Quality Assurance.

8.0 EXPERIMENTAL DESIGN:

8.1 LD50 Test:

<u>Test Article</u>	<u>Dose Level (mg base/kg)^a</u>	<u>Route of Administration</u>	<u>Number of Males</u>	<u>Number of Females</u>
WR269410	TBD	Oral	5	5
WR269410	TBD	Oral	5	5
WR269410	TBD	Oral	5	5
WR269410	TBD	Oral	5	5
WR269410	TBD	Oral	5	5
WR269410	TBD	Intraperitoneal	5	5
WR269410	TBD	Intraperitoneal	5	5
WR269410	TBD	Intraperitoneal	5	5
WR269410	TBD	Intraperitoneal	5	5
WR269410	TBD	Intraperitoneal	5	5
WR242511	TBD	Oral	5	5
WR242511	TBD	Oral	5	5
WR242511	TBD	Oral	5	5
WR242511	TBD	Oral	5	5
WR242511	TBD	Oral	5	5
WR242511	TBD	Intraperitoneal	5	5
WR242511	TBD	Intraperitoneal	5	5
WR242511	TBD	Intraperitoneal	5	5
WR242511	TBD	Intraperitoneal	5	5
WR242511	TBD	Intraperitoneal	5	5

^aTBD = To be determined (WR242511 doses will be expressed as mg base per kg).

The number of animals in each group is necessary for statistical analyses.

Doses will be selected from range-finding study data in which 5 groups of 2 animals/sex/dose will be routinely used (Section 8.6).

- 8.2 Procedure to Control Bias during the Assignment of Animals to Treatment Groups: The animals will be randomly selected, within sex, using a table of random numbers or a computer-generated randomization program. The specific procedure will be documented in the raw data.
- 8.3 Frequency and Route of Administration of Test Article: Five groups of five animals/sex will receive a single dose of the appropriate test article by intraperitoneal injection or gavage as shown in Section 8.1. Dosing volumes will be constant on the basis of body weight and will be routinely 1 or 5 ml/kg (ip), and 5 or 10 ml/kg (oral). The specific dosing volume (ml/kg) will be constant throughout each phase of the study and will be documented in the raw data. Rats which are dosed by gavage will be fasted overnight (\approx 16 to 20 hours) prior to dosing. Food will be returned approximately 1 - 2 hours after dosing.
- 8.4 Justification of Route(s): The oral and intraperitoneal routes are convenient and accepted procedures for administering a specific amount of a test article to each animal, and is required by the Sponsor.
- 8.5 Test Article Vehicle: 0.5% Na⁺Carboxymethylcellulose/0.3% Tween 80.
- 8.6 Range-Finding Test: Initial oral and intraperitoneal range-finding doses of 25 mg/kg of WR242511 will be administered to separate groups of 2 animals/sex. This dose is approximately the oral LD50 determined in a previous acute toxicity study in rats (UIC/TRL Study No. 062). For WR269410, an initial range-finding dose of 800 mg/kg will be used for each route (2 animals/sex). This is the approximate intramuscular LD50 for this drug in mice as indicated by the Sponsor. No data for rats are available for this compound.
- Additional range-finding dose levels, routinely either twice or one-half the previous dose level, will be subsequently administered to groups of 2 animals/sex/appropriate route based on the previous results. Five range-finding doses/sex will be routinely administered for each drug by the appropriate route. The range-finding animals will be observed once daily for at least 5 days, and will be discarded when it is apparent that they will survive.
- 8.7 Test Article Dosage Form Preparation and Analyses: The stability and homogeneity of the test article/carrier mixtures will be determined prior to study start. Dosage formulations will be prepared by suspending the appropriate quantity of test article in the vehicle using a mortar and pestle. They will be analyzed for test article concentration prior to use, and only samples within 10% of their intended concentration will be used.

8.8 Type and Frequency of Observations, Tests, Analyses and Measurements:

8.8.1 Body Weight: Body weights of all animals will be recorded at test animal selection in Week -1, and on Days 0 (prior to dosing), 7 and 14.

8.8.2 Clinical Signs: All test animals will be observed for clinical signs at least three times after treatment on the day of dosing, and daily thereafter until termination. All pharmacologic and/or toxicologic effects will be recorded on an individual test animal basis. The animals will also be observed daily in the afternoon for moribundity/mortality during the two week holding period.

8.8.3 Postmortem Observations: All test animals which die during the 14-day observation period will be grossly necropsied as soon as possible. Those test animals that survive to Day 14 will be sacrificed by carbon dioxide asphyxiation and grossly necropsied on that day. The necropsy procedure will be a thorough and systematic examination and dissection of the animal viscera and carcass. A veterinary pathologist will be routinely available to verify gross lesions. All tissues and organs will be discarded following termination of the gross necropsy procedure.

8.8.4 Data Analyses: The incidence of all pharmacologic and/or toxicologic effects will be tabulated for each dose level by sex. For body weights, means and standard deviations will be calculated for each dose level by sex and time point. Probit analysis of dose-mortality data as described by Finney (1977) will be used to calculate the LD50 and its 95% confidence interval for each sex, and the slope of each dose-mortality curve.

9.0 RECORDS TO BE MAINTAINED:

All data generated during the conduct of the study, except those that are generated as direct computer input, will be recorded directly, promptly, and accurately in ink in bound books with prenumbered pages or on worksheets that will be bound during or at the conclusion of the nonclinical laboratory study. All appropriate computer and machine output will be bound during or at the conclusion of the study. All data entries will be dated on the day of entry and signed or initialed by the person entering the data.

Any changes in entries for whatever reason (e.g., to correct an error or transposition) will be made so as not to obscure the original entry, will indicate the reason for such change, and will be dated and signed or

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identified at the time of data input. In computer driven collection systems, the operator responsible for direct data input will be identified at the time of data input. Any changes in computer entries for whatever reason (e.g., to correct an error or transposition) will be made in such a manner so as not to obscure the original entry, if possible, will indicate the reason for such change, and will be dated and the responsible individual will be identified.

All recorded data will be reviewed, signed, and dated by a knowledgeable person, other than the person making the entry, to assure adherence to procedures and to verify observations.

Upon completion of the study and submission of the final report, all raw data, documentation, specimens, test article reserves and other materials necessary to reconstruct the study will be stored in the TRL Archives maintained by Quality Assurance, unless otherwise specified by the Sponsor.

All changes or revisions, and reasons therefore, to this protocol once it is approved will be documented, signed by the Study Director and Sponsor, dated and maintained with the protocol.

10.0 REGULATORY REQUIREMENTS:

This study will be performed in compliance with the UIC/TRL Quality Assurance Program designed to conform with FDA Good Laboratory Practice Regulations and EPA Good Laboratory Practice Standards. The protocol for this study was approved by the UIC Animal care committee.

Will this study be submitted to a regulatory agency? Yes
If so, to which agency(ies)? U.S. Food and Drug Administration
Does the Sponsor request that remaining test articles be returned? Yes
Does the Sponsor request that samples of the test article/carrier mixture(s) be sent? No

11.0 REFERENCES

Finney, D.J., 1977. Probit Analysis, 3rd Edition. Cambridge University Press, Cambridge, England.

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12.0 PROTOCOL APPROVAL:

STUDY DIRECTOR:

Barry S. Levine 12/3/92
Barry S. Levine, D.Sc., D.A.B.T. Date

QUALITY ASSURANCE:

Ronald Schoenbeck 12/7/92
Ronald Schoenbeck Date

SPONSOR APPROVAL:

George Schieferstein 12-8-92
George Schieferstein, Ph.D. Date
Contracting Officer's
Representative (COR)

COMMENTS FROM THE COR:

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APPENDIX 8
Study Deviations

ACUTE ORAL AND INTRAPERITONEAL TOXICITY
STUDY OF WR242511 AND WR269410 IN MICE

Study Deviations*

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<u>Deviation Type</u>	<u>Specific Deviation</u>	<u>Effect on Study</u>
Protocol	The probit method of Litchfield and Wilcoxon (1949) was used to calculate LD50s because it is an accepted means to calculate dose-mortality curves.	None.
Protocol	WR242511 tartrate is incorrectly described in the protocol as an orange powder. The tartrate salt of WR242511 is a yellow powder.	None.
Protocol	WR242511 tartrate is incorrectly identified in the protocol by the in-house chemical number of 0930614 (which was previously assigned to the succinate salt). The tartrate salt of WR242511 was assigned the in-house chemical number of 1720614.	None.
Protocol	The WR269410 (intraperitoneal) dosage formulation for the 30, 60, and 250 mg/kg treatment groups were in excess or deficit of 10% of their target concentrations (Table 2).	None; The LD50 was calculated on the basis of the actual doses administered.

*The detailed "Deviation Reports" are contained in the raw data which are archive at the University of Illinois at Chicago, Department of Pharmacology, Chicago, Illinois.

The above deviations did not affect the integrity of the study.

Barry S. Levine, D.Sc., D.A.B.T.

Date